AMDD

10-year History and Beyond

American Medical Devices and Diagnostics Manufacturers' Association

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Foreword

The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) is celebrating its 10th anniversary. We express our deepest gratitude for the guidance and encouragement we have received from all those involved with us.

Since its inception in April 2009, AMDD has acted as an intermediary to the Japanese Government and related administrative bodies. It is an industry group consisting of approximately 70 Japanese corporations that handle medical devices and in-vitro diagnostics (IVD) with their headquarters located mainly in the United States.

Specifically, with the cooperation of related organizations, such as the Ministry of Health, Labor and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA), we have been particularly active in our efforts to eliminate the long-standing issue of device lag and to build a regulatory system that takes into account the characteristics of medical devices. Our work has led to the acceleration of the medical device review process, and device lag has been almost eliminated. In November 2013, our long-held vision of separating regulations on pharmaceuticals and medical devices was materialized as the enactment of the Pharmaceutical and Medical Device Act (revised Pharmaceutical Affairs Law), which took effect the following year.

From 2016, for further credibility and transparency of the organization, AMDD changed from a voluntary organization to a General Incorporated Association (GIA). As we made the change to GIA, we established AMDD's new mission, which is to provide valuable medical technology and information for the healthy everyday lives of people. Medical devices and IVD are not only utilized in the treatment of illness, but also in numerous other applications, such as prevention and improvement of conditions after treatment. As an industry group that delivers such medical devices and IVD to Japanese patients under our new mission, we continue to expand our activities.

Since 2017, we have been working on a policy recommendation called Value-based Healthcare to evaluate the value of innovation in medical devices and IVD, and some of our recommendations have been incorporated in a "challenge application". To that end, we have established a think tank called the AMDD Medical Technology Policy Research Institute, which works on policy recommendations.

This booklet "AMDD: 10-year History and Beyond" summarizes the past 10 years and outlines our road ahead. Along with a record of AMDD's main activities, it also summarizes the achievements of innovation over the last decade that have contributed to patient care in numerous disease fields. We would be grateful if you could spend time to read this booklet.

Toward the next decade, in cooperation with the Japanese Government and related academic and industrial organizations, while collaborating with the US government and the Advanced Medical Technology Association (AdvaMed), we at AMDD will continue our activities including policy recommendations to contribute to the development of better medical care in Japan. We look forward to your continued guidance and encouragement.

September 2019

Kosuke Kato
Chairman
American Medical Devices and Diagnostics Manufacturers' Association (AMDD)

Chapter
1

Prehistory to the AMDD (1990s - 2008)

US-Japan Economic Frictions Led to the Medical Device Issue

For the establishment of the AMDD in April 2009, Japan's high economic growth after World War II and the relationship between Japan and the United States played vital roles.

Going back to the 1980s when Japan-US trade tensions peaked, after post-war high economic growth as described in "Japan as Number One: Lessons for America" by American sociologist Ezra F. Vogel in 1979, Japanese products were dominant across the world. The United States, in particular, suffered from a trade deficit with Japan because of Japanese electronic products and cars. The United States tried to stem the appreciation of the US dollar and aimed to strengthen the Japanese yen through the 1985 Plaza Accord, but the trade deficit continued even after the Accord.

Prime Minister of Japan Nakasone and the US President Ronald Reagan agreed to initiate the market-oriented sector selective (MOSS) talks in February 1985. According to the Japanese encyclopedia, the MOSS talks were "a method to discuss the US products that were internationally competitive but could not enter the Japanese market in the Japan-US trade negotiations, with a view to open the market to those products for individual sector, and discuss causes of trade barriers." One of the sectors was pharmaceuticals and medical devices.

What then happened to MOSS talks in the US-Japan trade friction? For the answer, we can refer to an article in the Nihon Keizai Shimbun (Nikkei) dated April 22, 1990, titled "Follow-up MOSS meeting on Pharmaceuticals and Medical Devices in Tokyo after holidays." The article describes the meeting, where the two countries were to focus on official pricing of special treatment materials, such as pacemakers, and methods for calculating drug price standards. Nowadays, special treatment materials, such as pacemakers, are covered by the National Health Insurance and have official prices, but at that time there were no such official prices. For this reason, from April 1990, the Ministry of Health and Welfare created a policy for setting official prices for insurance claims. However, the setting of official prices had negative pressure on profits for the US manufacturers, which in turn led to criticism in the US of increasing trade imbalances. This further strained negotiations between the two countries. The Nikkei article dated July 15 reported that "for pacemakers, Japan relies almost 100% on imports, 90% of which are made in the US. Since medical institutions invoice the purchase price as insurance claims, even if manufacturers mass-produce medical devices, pricing pressure would not work." Therefore, "the Ministry of Health and Welfare plans to set official prices for insurance claims from April this year with the aim of lowering price levels."

The Establishment and Activities of the ACCJ Medical Devices / IVD Subcommittee

Under these circumstances, the Chemical Daily, dated April 9, 1993, reported that an expert committee on special treatment materials at the Central Social Insurance Medical Council (Chuikyo) met to exchange views with the representatives of the American Chamber of Commerce in Japan (ACCJ), the European Business Council (EBC), the Advanced Medical Technology Association (AdvaMed, formerly the Health Industry Manufacturers Association (HIMA)), and the US Department of Commerce. The aim was to summarize considerations regarding price ranges and revision rules for special treatment materials by June 1993. The basis for pricing was presented as an idea based on function; however, this was met with calls for it to be done by brand.

The Nikkei Sangyo Shimbun, dated August 13, 1997, reported that the Ministry of Health and Welfare released findings of its first distribution survey on medical devices on August 1. The survey showed that the price of pacemakers and PTCA balloon catheters (catheters for dilating the heart coronary arteries) increased from 1.2 times to 8 times that of Europe and the United States. Until then, the difference between domestic and foreign prices has been raised as problems by the Japanese side. There was also a report that foreign manufacturers were raising shipping prices to Japan. However, Leo Tilly, then Chairman of the ACCJ Medical Device Subcommittee (hereinafter "Subcommittee"), stated that his Subcommittee had argued that many of Japan's unique business practices and regulations are the cause of the high costs, and this survey proved that those claims were not wrong. He went on to say that the Subcommittee would continue to ask the Japanese Government for four deregulations. The newspaper outlines the fours deregulations; 1) Give preferential evaluation in medical insurance to medical devices with innovative technology (that allows

early treatment / discovery) because such devices can bring down medical costs, 2) Allow overseas data to be used as they are for clinical studies (clinical trials) in Japan, 3) Categorize IVD as medical devices because they are closely related to medical devices, unlike general drug products that are taken in the body, and 4) Shorten time to approval. Mr. Tilly commented in the article, "I question the simplistic view that if the price of medical devices goes down, the cost of medical care will go down. When the introduction of advanced devices is delayed because of tight regulations, complicated procedures and red tape, we cannot serve the patients."

Moreover, under the headline, "The Report by the ACCJ : slow penetration of medical technology, urging the acceleration of new product approval," the Nikkei Sangyo Shimbun dated September 17, 1999 reported that "According to the report, titled 'A Turning Point of the Japanese Healthcare System' (commonly known as the Bain Report), published by the Subcommittee, the implantable cardioverter defibrillators (ICD) that prevent sudden death due to arrhythmia, liquid medium for tuberculosis diagnosis, and artificial joints are not gaining ground in Japan, as compared with overseas, against the backdrop of the slow approval process and the low test fees. The Subcommittee stresses that the introduction of new technologies will lead to improved quality of life (QOL) for patients and reduced medical costs. Going forward, it will distribute reports to related organizations, such as the Ministry of Health and Welfare, and seek reform of the healthcare administration." This was the beginning of the Japanese "device lag" issue, a term for the slow time to approval, which was raised as a major issue (non-tariff barrier).

Originally, the Subcommittee was established within the ACCJ by Mitsuo Hirose, then President of J&J Medical (now Johnson & Johnson). Back then, he was watching discussions in the Japanese medical device industry group which tended to make requests centering on their interests, and he decided to set up an industry group for foreign medical device manufactures to independently express demands that are different from the Japanese industry group. He also served as an expert member of Chuikyo from 1999 to 2005 while belonging to the Subcommittee. (Since then, expert members of Chuikyo have been appointed from AMDD member companies. Please also refer to the round-table discussion article featuring past expert members on page 20 of this journal.)

Launch of Awareness Campaign, "the Role of Advanced Medical Technology"

HIMA (later changed its name to AdvaMed) that had worked with the US Government since the 1980s, and the Subcommittee (later changed its name to Medical device/IVD subcommittee) expressed concerns in 2000 that among all problematic issues raised up to that point, the country must take some sort of measures against the slow approval of new devices in the Japanese market and the official price cuts at the time of the revision of medical fees for special treatment materials. Otherwise, companies may find it impossible to continue business in Japan, which in turn would lead to a crisis that disadvantages Japanese patients.

In 1999, the previously mentioned Bain Report which was published in full by the Subcommittee, highlighted the contributions of special treatment materials, IVD, diagnostic imaging and other devices to Japanese healthcare and patients, and detailed that patients' QOL and reduction of medical expenses was brought about by technological innovation of medical devices amid the increased national medical costs. It was expected that proposed actions within the report would be seen by many government officials, and raised as an issue so that it would lead to the solution of the above-mentioned issues. However, the report wasn't widely picked up by the media, and did not seem to have significantly impacted government policy. This led to the realization that there might be problems with communication to stakeholders, including the media. Thus, a Task Force was launched by the main member companies of the Subcommittee. External communication, which up to that point had been handled internally, was to be carried out in concert with external experts.

The hired experts analyzed circumstances, and reiterated to the Task Force members: "Before talking about the issues of approval speed and the reduction of medical fees, we must first consider that nobody knows about medical devices and IVD. Even media do not know much except for trade papers. General papers and magazines fail to describe what constitutes medical devices (also known as medical instruments or equipment), and have no idea that the devices include not only injection syringes, surgical threads and needles, but also advanced medical technologies including pacemakers, stents and artificial joints that significantly contribute to life-saving procedures and improvement in post-operative QOL." Firstly, we must inform the general public of the role/value of advanced medical technology and of the presence of minimally invasive treatment that saves lives and contributes to the improvement of post-operative QOL. Secondly, we must explain why advanced medical technology is not gaining ground in Japan and keep appealing to the government although it may seem a roundabout approach.

These broad-based ideas led to the launch of the Value of Medical Technology: Public Awareness Campaign (hereinafter referred to as the Campaign). Preparatory work began in earnest in January 2002, and representatives of all member companies gathered on several occasions to be briefed on the purpose of the Campaign.

In 2001, the Subcommittee aimed to plan for external communication activities and set up a secretariat and appointed a staff director within the Subcommittee,

Dr. Yasuhisa Sakurai, Professor Emeritus, Tokyo Women's Medical University, gives a keynote speech at a press conference during the Value of Medical Technology: Public Awareness Campaign (October 2002)

Former Chairman of the ACCJ Medical Device / IVD Subcommittee, Dr. Huimin Wang, discusses issues of medical devices and IVD at a press conference (October 2002)

dedicated to industry activities and external communication, using funding from companies belonging to the Subcommittee.

The Campaign commenced with a message explaining the great value of advanced medical technology. Rather than the Subcommittee working alone, it called for a coalition of all stakeholders who support and promote such advanced medical technology within the industry. Minimally invasive advanced technologies improve post-operative QOL and shortens the length of hospital stays, and reduces medical costs. It was the solution to an issue of the Japanese healthcare system, and that was a major value of advanced medical technology.

As an endorser of the campaign, we asked for the cooperation of Dr. Yasuhisa Sakurai, Professor Emeritus at Tokyo Women's Medical University, and a leading figure in biomedical engineering in Japanese academia back then. He readily agreed to assume the role. At that time, Prof. Sakurai served as Co-Chair of the Medical Engineering Technology Industrial Strategy Consortium (METIS) which was established as a national strategy for Japanese medical devices, with Tsutomu Kanai, Chairman of Hitachi, Ltd. In addition, he served key positions in biomedical engineering such as the President of the Japan Society for Biomaterials and the Vice President of the Japanese Society for Medical and Biological Engineering. He also served as Chairman of the Society of Future Medicine, a representative of the Healthcare Research Park, and Chairman of a medical device industry roundtable for METI. He himself was also frustrated by the lack of recognition and understanding of medical devices, which play an equally important role as pharmaceuticals in Japanese healthcare, and thus, he was actively involved in the Subcommittee's campaign.

In this way, the Subcommittee built its key message, prepared materials to convey the value of medical devices and held many discussions with various stakeholders. In October 2002, a press conference was held for the launch of the Campaign at the Imperial Hotel in Tokyo. Professor Yasuhisa Sakurai gave a keynote speech on the value of medical devices. Dr. Huimin Wang, then Chairman of the Subcommittee (later the first Chairman of the AMDD) explained the purpose of the awareness campaign. Over 50 people attended the press conference, including industry news media, economic media and general newspapers, and journalists, in addition to other related parties. A sense of expectation was in the air that something new was on its way. Because minimally invasiveness is a value of medical devices that improves patients' postoperative QOL, a QOL campaign logo was also unveiled at the press conference, and covered in articles on the following day.

わたしが選ぶ［わたしの医療］
Value of Medical Technology
QOL
Quality of Life

The campaign's primary purpose was to raise awareness and understanding of medical devices and IVD among the general public. The strategy was to conduct a series of media lectures, and use examples of the latest advanced medical technology to promote its value to patients. However, the message the Subcommittee was to send was not a promotion of individual company products, but rather a representation of their product categories.

Unlike pharmaceuticals, the advanced medical technology, therapeutic devices such as pacemakers, ICD, artificial joints, artificial heart valves, stents, diagnostic imaging technology, and IVD were not something patients used on a daily basis. Patients were not familiar with devices used for their surgeries, while the general public's recognition and understanding of such technology was even further from sufficient.

The first lecture of the media lecture series started in February 2003, looking at mammography for early detection of breast cancer as a representative example of diagnostic imaging. In those days, the incidence of breast cancer, mainly among young women, was increasing and awareness of breast cancer was growing through the Pink Ribbon Movement. The lecture attracted great interest. The media lecture was attended by breast cancer patient groups and

Words from the Chairman

Former Chairman on 10 Years of the AMDD

Huimin Wang, First Chairman (2009 - 2010)

It was in 2002 when I became Chairman of the ACCJ Medical Devices and IVD Subcommittee (hereinafter "Subcommittee"), the predecessor of the AMDD. In the same year, Edwards Lifesciences Ltd, which I currently lead, spun off and became independent after taking over the cardiovascular product business of Baxter Ltd. For several years the Ministry of Health, Labour and Welfare (MHLW) had already considered the "issue" of so-called internal and external price differences when overseas medical device manufacturers sold their products in Japan. The MHLW had surveyed the prevailing market prices in other countries and was considering the introduction of a foreign average price (FAP) system to adjust the prices of those items whose price was significantly different from the average. This was an extremely big challenge for us, and the Subcommittee had considerably heated discussions with the MHLW concerning the value of medical devices.

During this period, Bob Hurley, President of Baxter, who was my boss and Chairman of the Subcommittee, asked me to accompany him to the MHLW as an interpreter. He stood in front of the director's desk and started to express his opinions of the domestic and foreign price differences. As I was interpreting, we were told, "I understand what you are saying, but make an appointment next time." I was very surprised that he had not even made an appointment. It was such a huge challenge to deal with this "issue". Unfortunately, the FAP system was introduced in April 2002 and is still in place today.

I took office as Subcommittee Chairman amid such turmoil, and there was a lot to tackle. With a paper on direct investment in Japan at the ready, I visited and had heated discussions with numerous related organizations and parties, including the MHLW, concerning aspects such as the need to eliminate the Device Lag, which was a major issue along with FAP at that time. This was eventually taken up by the Council on Economic and Fiscal Policy and led to a bold policy to eliminate the Device Lag. This ultimately developed into the Medical Device Review Acceleration Action Program at the MHLW. During this process, the division in charge at the MHLW often requested me to provide detailed data and papers by midnight of the same day for the various recommendations that we advocated. I am very much indebted to my assistant at that time, who helped me late into the night on many occasions.

Then came a problem with governance. We were informed that the ACCJ's proposals and other submitted documents must be approved by the board of directors. Organizational governance is naturally expected but strict adherence may have stymied and halted some industry activities. I discussed the issue many times with the ACCJ executives, but they did not come around to my way of thinking.

I had a strong conviction that it would be better to act independently of each other and communicated this conviction to the heads of the main member companies of the committee, and most of the members agreed. We prepared ourselves for independence and the current AMDD was established on April 1, 2009. I served as the inaugural Chairman.

Masataka Toyota, who acted as Staff Director at the Subcommittee, visited member companies with me to explain this independence. And he worked tirelessly to create a foundation for the new organization, including negotiating to transfer the budget for activities from the ACCJ Subcommittee to the new organization, enacting a new organizational name and CIs, and creating the articles of incorporation. I am very grateful to him.

The AMDD has matured as an organization in the 10 years since its inception. There has been no such dramatic change as when the FAP system was introduced, and the medical device approval system has improved considerably. It seems as if there is a lack of a sense of crisis as in the ACCJ era. However, the risk remains that the recent changes to the Japanese healthcare system may cause some companies to forego the introduction of new products in the near future. Now we must think about what we can do as suppliers of medical devices and IVDs. We can present a bigger vision: how the medical system should be amid Japan's declining birth rate, aging population, and the security of medical finances; and how medical devices should be positioned against such a background. These are visions from a broader perspective: we should state that medical devices and IVDs will demonstrate their true value by improving treatment quality and patient QOL and explain how we want their value to be appropriately evaluated.

I believe that one of the important roles of industry groups is to present larger visions that make Japan healthier.

(Corporate Vice President, Japan, Asia and Pacific, Edwards Lifesciences)

Pink Ribbon representatives. Subsequently, the media lecture series, which introduced advanced medical technologies step-by-step, continued intensively for two years; once every two months (26 times to date). A media forum that focused more on healthcare issues, and a patient symposium, titled Toward Patient-Centered Medical Care (breast cancer, diabetes, pacemakers) were held. At each event, Professor Yasuhisa Sakurai's lectures on the value of medical devices and IVD from an academic standpoint plus the Q&A sessions, helped to deepen the media understanding of

Toward Patient-Centered Medical Care symposium (October 15, 2004), attended by patient group representatives

advanced medical technologies, which significantly contributed to raising awareness (these presentation materials can be found on the AMDD website).

Approval Speed of Advanced Medical Technology

In the 2000s, a social problem surfaced: there was a time lag of several years before drugs developed and approved overseas (particularly anticancer drugs) were approved by the MHLW in Japan. This is called a drug lag. The same thing happens with medical devices and IVD, and this is called a device lag. In particular, the approval review system was inadequate. Even though there were many drug reviewers, those dedicated to medical devices were limited, and this caused a delay in approval, thereby creating a device lag. The Subcommittee surveyed how far the approvals of medical products of the Subcommittee members were delayed, causing the device lag, so that they could actively advocate for government policy change. The survey results were published in October 2008 as the "2008 Device Lag Survey" known as the Device Lag Report. In December 2008, the Subcommittee held a press conference on the subject.

On the heels of the Device Lag Report, the media (newspapers, magazines and TV) that had mainly covered the benefits of medical device, including lifesaving advantages and improvements to patient QOL, began to report intensively that the latest medical devices reach the Japanese market several years after they have been marketed overseas, and those devices are two or three generations old, placing Japanese patients at a disadvantage. Thus, "Device Lag" became a buzz word in the media. Intensive media coverage continued from 2006 to 2009 when the AMDD was established. But what triggered the buzz was a seven-part series in the evening edition of the Asahi Shimbun, titled, "Seven Wonders of Japan's Medical Devices." The article was written by Isao Tanabe, who was a staff writer for the paper's healthcare and medical section. He strongly voiced concerns over the slow approval of medical devices and the lack of actions from the administration to accelerate the approval process in Japan. This gave a big impact, not only on the medical device industry, but also on the healthcare administration. In December 2009, Subcommittee Chairman Huimin Wang and Vice Chairman Jean-Luc Butel held a press conference as the Subcommittee published a Viewpoint, titled, "Improve Patient Access to Advanced Medical Technologies."

Meanwhile, aside from the Subcommittee, the Foreign Direct Investment (FDI) Task Force established within the ACCJ announced in their Viewpoint in March 2004 that the delay in approval of medical devices would alienate foreign direct investment into Japan, which would be a big blow to the Japanese economy. ACCJ FDI Task Force and Subcommittee members explained this Viewpoint to various key opinion leaders who were influential to the Japanese healthcare system. Haruo Shimada, an economist who was one such opinion leader, noticed this Viewpoint when he was President of Chiba University of Commerce and Chairman of the Cabinet Office Invest Japan expert panel. The device lag issue was on the agenda of the Council on Economic and Fiscal Policy, and was included in the Government's basic economic and financial policy, or 'Honebuto' Policy, which was compiled in June 2008. This led to the formulation of the Medical Device Review Acceleration Action Program aimed at eliminating device lag in the MHLW. Please refer to Chapter 2 and subsequent chapters for details on the device lag issue, which paved the way for a major change in Japan's approval system, and led to collaboration with the MHLW / PMDA that resulted in revisions to the Pharmaceuticals Affairs Law in respect to medical devices.


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Asahi Shimbun, February 4, 2006, evening edition

Contribution

What I have Witnessed in 10 Years of the AMDD

Masataka Toyota, First Staff Director

Congratulations on 10 years of the AMDD. I served as Staff Director for nine years from July 2003 to March 2012. Seven years have passed since my retirement, and I currently devote my time exclusively for local volunteer activities. However, I can say I had the most joyful and fulfilling time of my life in that position.

I remember clearly when I went to have an interview with Dr. Huimin Wang, then Chairman, accompanied by Yasushi Hirano who was my predecessor and a colleague in my previous job. Dr. Huimin Wang, Edwards Lifesciences President, and ACCJ Committee Chairman, was 15 years younger than I. However, he was a very pleasant man of integrity; his position didn't go to his head, and he didn't waste his words, and he always wore a smile. He said to me, "This job is about protecting the health of the people." That brought home just how noble the job is. At the same time, the working environment seemed to respect people with ability, regardless of age, so I was eager to work there. Throughout my nine years there, these notions were my motivations.

The major event during my tenure came when the AMDD became independent of the Subcommittee at the ACCJ 10 years ago. ACCJ is a huge organization which represents all American industries, including aircraft, finance and agricultural products. For the smooth operation of the organization representing broad sectors, strict rules were in place that all external documents should be checked in advance. The Medical Devices and IVD Subcommittee was frequently required to submit documents to the MHLW, and Japanese documents had to be translated into English on each occasion, then have them checked by the ACCJ. However, in reality, circumstances were often more difficult because the government demanded that documents be submitted by the following morning. There was immeasurable relief and benefits to be affiliated with the ACCJ, but after consultations with various parties, it was decided that it would be better to be independent for speed and efficiency. In preparation, we visited each relevant organization, including the ACCJ, the MHLW, the US Embassy, AdvaMed, and related industry groups, not to mention all the member companies, to explain carefully our decision and gain their understanding. As we transitioned to a new organization, we were faced with difficult challenges, such as naming the new organization and transferring the membership fee balance collected by the Subcommittee to the new AMDD. Everything was completed safely utilizing professional companies and thanks to the cooperation from the ACCJ.

Here we are 10 years later, and I'm overjoyed to say that the AMDD continues to develop as an important industry group for medical devices and in-vitro diagnostics (IVD), while fulfilling its mission to deliver the world's most advanced medical technology to Japanese patients. My hope is that the organization will continue to prosper while protecting the health of the people for the next 10 years, or the next 10 decades.

Inaugural AMDD board meeting, after being founded in April 2009

Cardiovascular Surgery (Heart Valve Thoracotomy and Catheter Surgery)

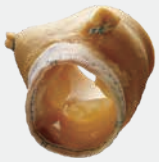
The heart is divided into four chambers. Four valves keep the blood flowing in one direction. Problems in the function of these valves are known as valvular heart disease. Valve replacement surgery, one surgical treatment for valvular heart disease, is to remove a deteriorated valve from a patient and replace it with a biological or mechanical valve. Since the first valve replacement surgery in 1952, a number of artificial heart valves have been devised as technology has advanced. In the same way, surgical techniques themselves have advanced remarkably, and valve replacement surgery is now a very common procedure. In recent years, minimally invasive treatment methods with less impact on a patient's body, are gaining ground.

History of artificial heart valves

Basic research into artificial heart valves began in the 1940s, and in 1960 ball valves were marketed as the first artificial heart valve products.

Two-leaf valve

Subsequently, a thinner, disc-shaped valve (referred to as a mechanical valve) was developed and replaced the ball valves. Currently, the mainstream mechanical valves are two-leaf models which are highly durable and widely used across the world.

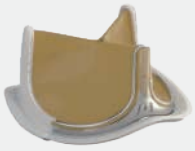


Stentless biological valves fabricated from porcine aorta

Artificial heart valves also include tissue valves made from biological materials.

In 1956, a donated human valve was collected for treatment using a homograft (homogeneous valve) in which the valve is transplanted into the descending thoracic aorta of a patient with aortic regurgitation. However, homografts are difficult to obtain. As an alternative, porcine valves with stents; porcine aortic valves that are inserted into three stents, came into clinical use. In the 1970s, a bovine pericardial valve with stent; bovine pericardium, was used for the leaflet, came into clinical use.

In the 1990s, a stentless tissue valve processed from a porcine aorta was developed and is still in use after a number of improvements. Long-term durability has been a challenge for biological valves, but improvements in structure and methods of fastening leaflet tissue, especially in the 2000s and later, have accelerated better design and calcification suppression treatment, further improving hemodynamics and durability. Moreover, tissue valves that use metal-free stents and tissue valves that have the function of expanding the annulus frame has been developed in anticipation of new treatments. The ever-evolving tissue valve is used across the world to treat valvular heart diseases.



Tissue valves that expand the annulus frame

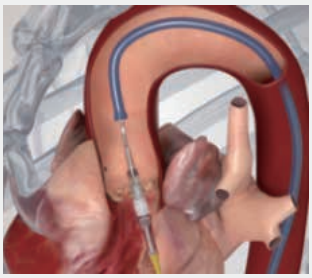
The evolution of surgery and minimally invasiveness

Surgical procedures also continue to evolve. Usually, in valve replacement surgery, a sternal incision is made to open the ribs and approach the heart. However, from around 2000, minimally invasive cardiac surgery (MICS) that makes a smaller incision to approach the heart has been introduced. In addition, surgery using thoracoscopes and surgical robots is also being introduced for the treatment of valvular heart disease.

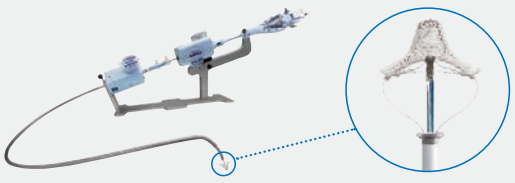
In 2002, Alain Cribier and his team made the world's first successful clinical use of transcatheter aortic valve implantation (TAVI), in which a tissue valve was placed in a human without opening the chest. Since then, a number of improvements have been made in tissue valves for TAVI. Now the established method is to crimp a tissue valve to the tip of the catheter, transport it to the valve position mainly through a small incision in the leg and place the tissue valve. The method is now widely used in the world, particularly on patients for whom open heart surgery is not an option.

The arrival of TAVI gave rise to a new treatment method; TAV in SAV (also known as Valve in Valve). For those patients who have already undergone valve replacement surgery using a tissue valve, but subsequently need a second valve replacement, this new method allows the placement of the second tissue valve through the catheter without another open heart surgery. It is very advantageous for patients since they can select treatment without another open heart surgery because tissues once incised through surgical procedures often fuse, making it difficult to conduct a second surgery.

In the treatment of valvular heart disease, valve repair is widely performed to shape the valves. Various types of annuloplasty rings and bands are used for atrioventricular valves such as mitral valves. Catheter treatment is now clinically available in the field of valve repair, using a catheter to approach the valve and form the valve by pinching the leaflets with a clip-shaped device.



Transcatheter aortic valve implantation (TAVI)



Procedure to form a valve by pinching the leaflets with a clip-shaped device

Increased therapeutic and product options allowed the selection of the optimal artificial valve and optimal treatment method for an individual patient's condition. In addition, the development of less invasive treatments and medical devices that make them possible, contribute to an improvement in quality of life (QOL) by reducing the burden on patients, such as fast post-operative recovery and less conspicuous surgical scars.

Cardiac Implantable Electronic Devices (CIED)

CIED is the common name for cardiac implantable electronic devices. One of the epoch-defining events in the past 10 years was the emergence of MRI-conditional devices. Conventionally, CIED covered by metal cases were contraindicated for MRI. MRI was used more frequently in Japan than in Europe or the US, and there were great expectations from healthcare professionals. Companies spent an enormous amount of time and energy to develop a device and a test method to assess the impact on CIED units and leads, and to secure and demonstrate patient safety during MRI scans. Discussion of further validation methods will be necessary in accordance with MRI advancements such as higher resolution.

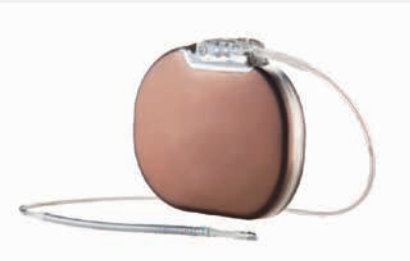
The second major innovation was the development of leadless devices. The benefits of a leadless pacemaker include the elimination of infections associated with the implanting procedure of pacemakers with leads; and there is no chest protrusion from the traditional pacemaker implantation technique, where the device is placed in the heart chamber, thus freeing patients from cosmetic and lifestyle restrictions. The concept of leadless pacemakers has been present since the 1970s, but it was not technologically feasible until recently. The concept was created as a result of the integration of numerous technologies, including miniaturized electronic circuits and batteries, electrodes that stimulate the myocardium tissue lodging mechanisms, sensors that distinguish between body movements, heart movements and enabling MRI.

Additionally, a subcutaneous implantable cardioverter defibrillator (S-ICD) system was developed; it can perform shock treatment in a similar fashion to the ICD system, without placing a lead in the heart. Because the S-ICD system does not place leads into blood vessels, clinical results show a decrease in the incidence of intravascular infection, and that of heart perforation and pneumothorax during the implantation procedure that intravenously places a lead. As such, it is expected to improve patient prognoses. The S-ICD is also MRI-conditional, therefore post-implantation workup is possible.

The third innovation was the inclusion in CIED of implantable devices that are not therapeutic devices but have diagnostic functions only. They were expected to monitor cardiac rhythm and to demonstrate the ability to detect arrhythmia, particularly atrial fibrillation, and are used to investigate the cause of cryptogenic stroke and to diagnose syncope with unknown causes. As they were not treatment devices, it was imperative that CIED be particularly small in size for Japanese who are resistant to invasive implantation of foreign objects in their bodies. After much hard work, the current sized device resulted. At the end of 2018, the Basic Act on Measures against Stroke and Cardiovascular Disease came into effect, making the prevention and effective treatment of stroke and cardiovascular disease national policy. Since atrial fibrillation is a major cause of cerebral infarction and a factor of incidence and aggravation of heart failure, the role of devices that continuously diagnose and monitor heart rhythm 24/7 is expected to increase.

New fields that we expect to see in the next 10 years include telemedicine, patient monitoring, and prognostic improvements using AI and IoT. While Japan's declining birthrate and aging population squeeze the national budget and a longer healthy life-span is desired, there is a need for efficient medical care. Work-style reform of healthcare professionals is also urgent. Efficiency that does not compromise healthcare quality will be the responsibility of the entire healthcare industry. It is now deemed possible to collect biological information, including the heart rhythm of a patient, and process and analyze the data, then use it to constantly monitor the patient's condition, and give warnings or suggestions for improvement.

The collected information can then be linked to more sophisticated external AI and IoT. By connecting it to physicians and patients, we can create a world in which immediacy and convenience are enhanced, and efficiency is enabled. With increasing public awareness of health, self-management of health through wearable devices such as smart watches will increase. Heart rhythm monitoring with a wrist watch device is also becoming feasible, and this may allow patients to present data in the future, which are used by medical institutions. To that end, a number of issues need to be addressed, including: information security; establishment of a system for collaboration between clinics, hospitals, and medical institutions; challenges of healthcare economy; and data reliability. To stay up to date, the promotion of collaboration among industry, academia, hospitals, and government must be planned for the next 10 years.



Subcutaneous implantable cardioverter defibrillator (S-ICD) system

Leadless pacemaker

Implantable ECG recorder

Chapter
2

Device Lag: History from Conflict to Dialogue – Near Revolutionary Reforms at the PMDA

On August 26, 2008, Dr. Tasuku Honjo, who at the time was a member of the Council for Science and Technology, participated in a "Public-Private Dialogue on Innovative Drug Discovery". There he stated that reforms close to a revolution would be necessary to deliver the latest medical devices and medicines to the Japanese people ahead of the rest of the world.

1. Request to increase the number of PMDA reviewers

"If the number of reviewers is increased, the number of inquiries will increase accordingly, so we are fine with things as they are," responded the ACCJ Medical Devices and IVD Subcommittee (hereinafter ACCJ) when asked if the number of PMDA reviewers for medical devices should also be increased in a similar manner as when the MHLW increased the number of PMDA reviewers for pharmaceuticals in the latter half of 2006.

A year later, the Director of the Evaluation Management Division at the Pharmaceutical and Food Safety Bureau (now Pharmaceutical Safety and Environmental Health Bureau) and the Director of the Medical Device Evaluation Division were again before the ACCJ, asking to "increase the number of reviewers." The ACCJ stated that it would first seek to set out the necessary conditions rather than simply accepting the increase in reviewers and costs. During a preparation period of about one year, we published the 2008 Device Lag Survey (October 2008)[1]. Excerpts from the recommendations are shown below.

2. Device Lag Survey

The device lag survey impacted numerous areas. In 2008, the ACCJ conducted the "Time Clock Survey" (survey period: April 2005 to March 2008), which found that, compared with the US, device lag in 2008 was about 2.9 years for new medical devices (PMA[1] equivalent 29 items), and about 3.6 years for products other than new medical devices (510 (k)[2] equivalent 126 items).

When the average total review period was compared between Japan and the US, the results were as follows (the average total review period of the US FDA follows in parentheses):

1) New medical devices (PMA): 21.1 months (10.1 months)
2) Products other than new medical devices (510 (k)): 14.3 months (2.2 months)

Review period by reviewed area and the comparison with the US are summarized in **Figure 1**. Although there were variations depending on the area, no review period in Japan was shorter than that of the US. We can see many fields with no difference between new medical devices and generic ones, or where the difference is not as distinctive as in the US. This is presumed to be an adverse effect of the same reviewers examining new medical devices and generic versions in Japan. The PMA and 510(k) review tracks are separate in the US.

Recommendations for shortening review periods

1. The Least Burdensome Approach will be introduced as the underlying philosophy and principles for reviews and consultation thereof.
2. For consulting on and reviewing improved devices and generic versions, only the minimum necessary information will be requested to determine Substantial Equivalence.
3. The PMDA will set a performance goal every year, which should be shown in a percentile method to secure accurate predictability of the timing of product introduction. In the future, the approval cohort should be switched to an application cohort so that the reform results are consistent with performance.

Recommendations for the recruitment of reviewers and training

1. When hiring reviewers, they should be actively hired from the private sector and assigned according to man-hours.
2. Introduce systematic education programs for improvement related to reviewers' product knowledge and technique related to review. The ACCJ will also cooperate.
3. The ACCJ and other medical device organizations will provide venues for seminars to raise the quality of all applicants.

[1] PMA: Pre-Market Approval, high risk Class III review process

[2] 510 (k): Also called Premarket Notification. It comprehensively evaluates the substantial equivalence (purpose of use, technical specifications, efficacy) and safety of devices in comparison with those that are legally marketed in the US, and approves domestic marketing of medical devices in the US.

3. Formulation of Accelerated Review Action Program

In response to recommendations from the May 20, 2008 meeting of the Invest Japan expert panel and with the support from the 'Honebuto' Policy approved by the Cabinet on June 27, 2008, the Medical Device Review Acceleration Action Program began in earnest on December 11, 2008. The outline is shown below. Almost all of ACCJ's proposals were accepted. Medical device groups, including the ACCJ, received approvals ahead of time to increase commissions, which serve as funds for additional reviewers, under the condition that the contents of the recommendations were achieved. The IVD industry group did not agree with this policy, and therefore, this was not included in the action program. However, an action program specializing in IVD was later formulated and achieved similar results.

It was also agreed progress would be checked at a biannual review meeting.

1. Improve quality by increasing the number of reviewers (phased increase from 35 to 104) and by bolstering training
2. Implement a three-track review system (new / improved / generic)
3. Clarify review criteria
4. Establish a standard total review period (median), progress management
   - New medical devices (conventional): 14 months
   - New medical devices (prioritized): 10 months
   - Improved medical devices (with clinical data): 10 months
   - Improved medical devices (without clinical data): 6 months
   - Generic medical devices: 4 months

4. Heated debate at Action Program Review meeting

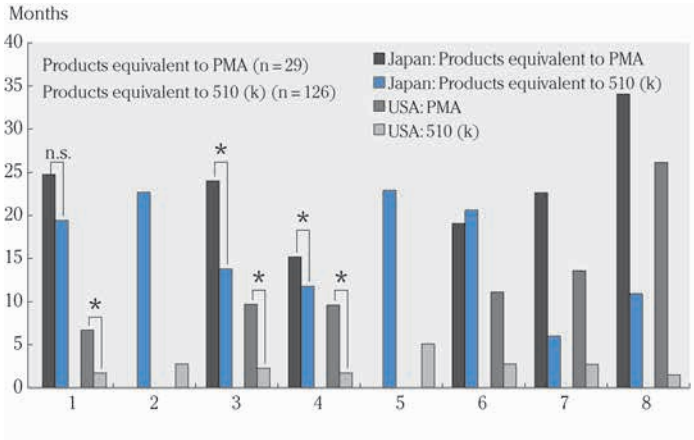
In December 2009, the first review meeting was held. Japanese organizations were quick to claim that reviews were slow and the reviewers were incompetent, but the PMDA responded by claiming the quality of applications was poor and the writing was illegible. Despite the fact that the tenor of the meeting was far from typical, it was impressive to see that the Director of the Office of Medical Device Evaluation Division was calm and collected in addressing the situation. The MHLW served as a buffer during the heated debate.

The AMDD had initially requested that the PMDA disclose performance data, but the request was declined. Thus, the industry group continued to seek improvements by presenting its own results from the Time Clock Survey (**Table 1**). At the time of the 2008 survey (the foundation for the Device Lag Survey), participating companies (all ACCJ members) numbered only 43. Subsequently, the EBC and the Japan Federation of Medical Devices Associations (JFMDA) agreed with the significance of the industry collecting its own data. As of 2012, 219 of the 347 member companies responded (63% response rate), covering 702 of 1,213 approved items (PMDA data), which accounts for approximately 60% of the total. With that, we were able to confront the PMDA with overwhelming evidence. As a result, the PMDA gradually began to disclose performance data, eventually making it possible to exchange constructive opinions.

Table 1. Time Clock Survey conducted by AMDD during the Action Program

Time of survey	Survey period	Organization	Number of participating companies
2008	April 2005 onwards March 2008	ACCJ Medical Device and IVD Subcommittee (Now AMDD)	43 companies
2010	January 2008 onwards December 2009	AMDD, EBC, JMED (now MT Japan)	214 companies
2011	January 2010 onwards December 2010	AMDD, EBC, JFMDA	269 companies
2012	January 2011 onwards December 2011	AMDD, EBC, JFMDA	219 companies

EBC: European Business Council in Japan
MT JAPAN: Medical Technology Association of Japan
JFMDA: The Japan Federation of Medical Devices Associations



Field		1	2	3	4	5	6	7	8
n	Items equivalent to PMA	6	0	7	10	0	1	4	1
	Items equivalent to 510 (k)	6	3	21	20	7	25	12	32

n.s.: Not significant ＊: $p<0.05$

Field 1: Mainly ophthalmology, otolaryngology; Field 2: Mainly dentistry; Field 3: Mainly cerebral circulation, respiratory system, neuropsychiatry (material system); Field 4: Mainly cerebral circulation, respiratory system, neuropsychiatry (mechanical system); Field 5: Mainly digestive system, urinary system, obstetrics and gynecology related fields; Field 6: Mainly orthopedics, plastic surgery and dermatology related fields; Field 7: Mainly clinical laboratory tests (related to drugs for in-vitro diagnosis); Field 8: Mainly multi-field medical devices, high-level medical electronic devices and medical devices not belonging to other fields

Note: In fields 2, 5, 6, 7 and 8, the number of samples was not sufficient and significant tests could not be performed.

Figure 1. Comparison of review periods by review field: PMA equivalent products vs. 510 (k) equivalent products

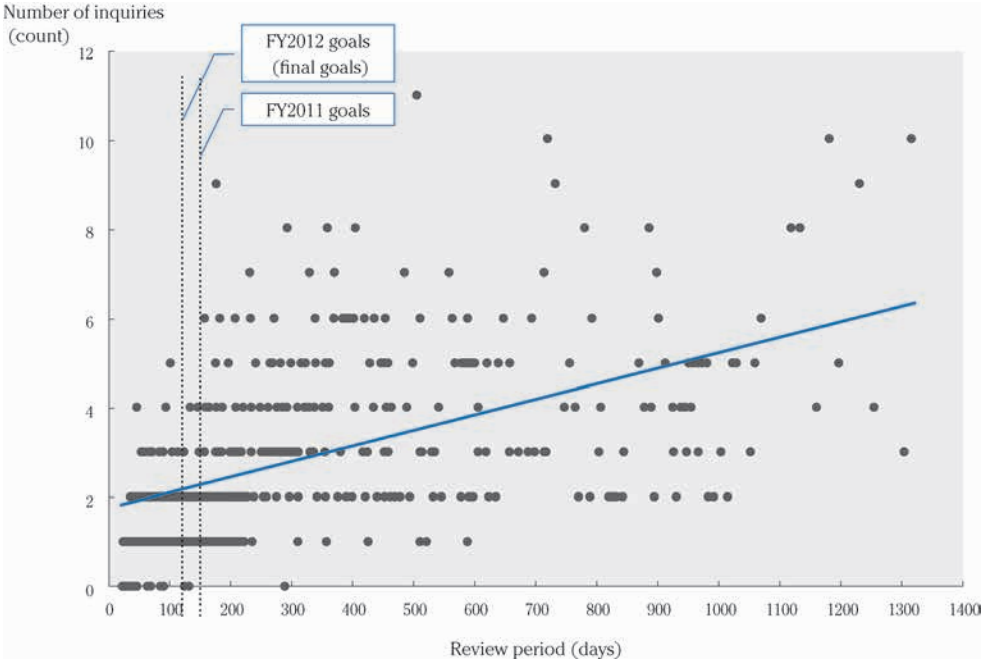


Figure 2. Relation between the number of inquiries for generics and the total review period (including partial change applications)

5. Two Obstacles Hindering Success: Generics Reviews and Backlog:

1) Generics reviews [3]

Team reviews were conducted on new and improved medical devices, and improvement began to be noticed to a certain extent. However, no improvement was noted in generics. To investigate the cause, the correlation between the number of inquiries and the review period was examined using data from the 2011 Time Clock Survey (**Figure 2**).[3] The dots to the right of the performance goal lines, represented by the dotted lines, are items that were not approved within the overall review period for the items. Although individual circumstances are not known, it is surprising that in one case for a generic, the total screening period was 1,300 days and included 11 inquiries. For generics it was requested that the number of inquiries be limited to 1 to 2 or at most 3.

In response to this, the PMDA implemented a Buddy System (a system that pairs experienced reviewers with inexperienced ones) in April 2011 for the review of generic medical devices. While at the same time, the field barrier was also eliminated to level out the variation across fields. Although the AMDD was grateful for the PMDA's initiatives for improvement, we determined that mindset was the most important factor in conducting generics reviews. For example, we recommended that reviews focus only on the differences in comparison with previously approved products, and that devices be evaluated in their entirety rather than by their raw material components, as in the case of pharmaceutical products.

The following quote[4] from the PMDA on September 2012 is about the Buddy System: "We could expect the effectiveness of the system in the case of a fully matured organization; however, in organizations where 68% of staff have less than 3 years of review experience, a lot of Buddies for new and semi-new staff will be produced. Additionally, the leveling of review standards across all fields also had a negative effect of raising the overall review level." Based on this view, the PMDA shifted its direction to the formulation of review standards that take into account the characteristics of each field.

2) Backlog [4]

Backlog was the most burdensome issue during the Action Program. Even though a number of initiatives had been implemented, considerable backlogs remained in field 2 (dentistry) and field 6 (orthopedics) (see **Figure 3**) at the end of 2011.

Backlog was the factor discouraging us the most. As long as backlogs remained, performance goals could not be achieved. We motivated ourselves and focused on solving the backlog issues by remembering that once it was resolved, performance would naturally improve.

6. Action Program results [5]

From the 6th Action Program Review meeting, held on July 24, 2012, the boxplot (**Figure 4**) proposed by the AdvaMed was adopted. It allowed us to instantly grasp the upper and lower limit proximity values, 25th, 50th, and 75th percentiles in the total review period.

Around this time, the PMDA released new data one after another. In particular, snapshot data were innovative since they clearly showed how many backlogged items existed and where they were.

Words from the Chairman

Former Chairman on 10 Years of the AMDD

David Powell, Second Chairman (2010 - 2012)

It was an honor to serve as AMDD's second Chairman, at a time when the members of AMDD were working closely with doctors, hospitals, governmental and bureaucratic leadership to reduce device lags and device approval gaps. Our goal was to ensure more people understood the unlimited potential of advanced medical technology and how such innovation could provide a substantial contribution to the reformation of the Japanese medical care system.

I very much appreciated the collaborative teamwork and leadership provided by all AMDD Board members, the AMDD staff and our member companies on the critical topics we addressed, especially during a period of significant currency valuation challenges. During this time, AMDD performed detailed data analyses, multi-national comparisons of medical device and diagnostics approval processes, various reimbursement schemes and shared these and other insights with MHLW, governmental and other policy makers and key opinion leaders. In addition to testifying to governmental committees and working groups, AMDD published various white papers in our effort to share our findings in a clear manner. With a primary and common focus to accelerate the approval process for new, valuable products into the Japanese medical system, even competing companies will put aside their differences in order to collaborate for the benefit of society.

With the deepest condolences to everyone affected by this tragic disaster, I was nevertheless very fortunate to see such collaboration become more impactful, when on Friday, March 11, 2011, the Great Tohoku Earthquake and tsunami struck off the coast of Japan. As Chairman of AMDD, it was very important that all member companies worked together and with key governmental officials and organizations to meet the critical needs of society, our healthcare system and of everyone directly affected by the earthquake, tsunami and resulting nuclear disaster. Former Chairman Wang-san, along with others, worked closely with myself and AMDD leadership to maximize our response.

Immediately after the earthquake and during the ongoing aftermath, AMDD and MHLW realized we needed to quickly create unofficial guidance related to the transport of medical goods through the nuclear zone, into and out of hospitals and clinics and how to handle product returns, in addition to other, never-before-experienced situations. It was a challenging time for society and an important time for my family and me to remain in Japan, to ensure I was able to continue working closely with other AMDD and government leaders, as well as everyone in my company.

I am proud and thankful to have been a part of AMDD during its formative years and to have worked with so many strong, cooperative leaders throughout society. We were able to see the device gap and device lag shrink and begin the journey of ongoing improvement. I share my deepest appreciation to everyone who worked hard to help me succeed and to help me learn about the wonderful aspects of Japan's healthcare system and society. I wish great success for AMDD as it enters its second decade.

As a result of joint efforts of the PMDA and the applicants, the backlog was resolved. In the 9th Action Program Review meeting (final meeting) on December 17, 2013, it was confirmed that all data had shown improvement over 5 years as compared with the figures at the time when the Action Program was initiated. Table 2 compares the results of the total review period in 2009 and 2013 for the improved (without additional clinical studies) and generics categories. Data for new and improved medical devices (with additional clinical studies) are omitted because they include partial change applications known for extremely short review periods.

Figure 5 shows the transitions of generics review period using a boxplot. Not only the median is improved, but also the height of the box gets lower and the whiskers become shorter, indicating less variation. It shows that backlog was intensively cleared in the 2nd year.

However, the 50th percentile is insufficient in terms of approval predictability. Therefore, the Collaboration Plan for Medical Device Review Acceleration (FY2014 - 2018) was started in April 2014 for another 5 years. The theme was to improve the quality of reviews and applications,

Table 2. Comparison of improved (without clinical studies) and generics total review periods in 2009 and 2013

Application category	2009 (at the start)		2013 (in the end)	
	Target	Results	Target	Results
Improved (without additional clinical studies)	11 months 50th percentile	13.2 months 41%	6 months 50th percentile	6.9 months 50%
Generic	8 months 50th percentile	12.9 months 36%	4 months 50th percentile	3.5 months 59%

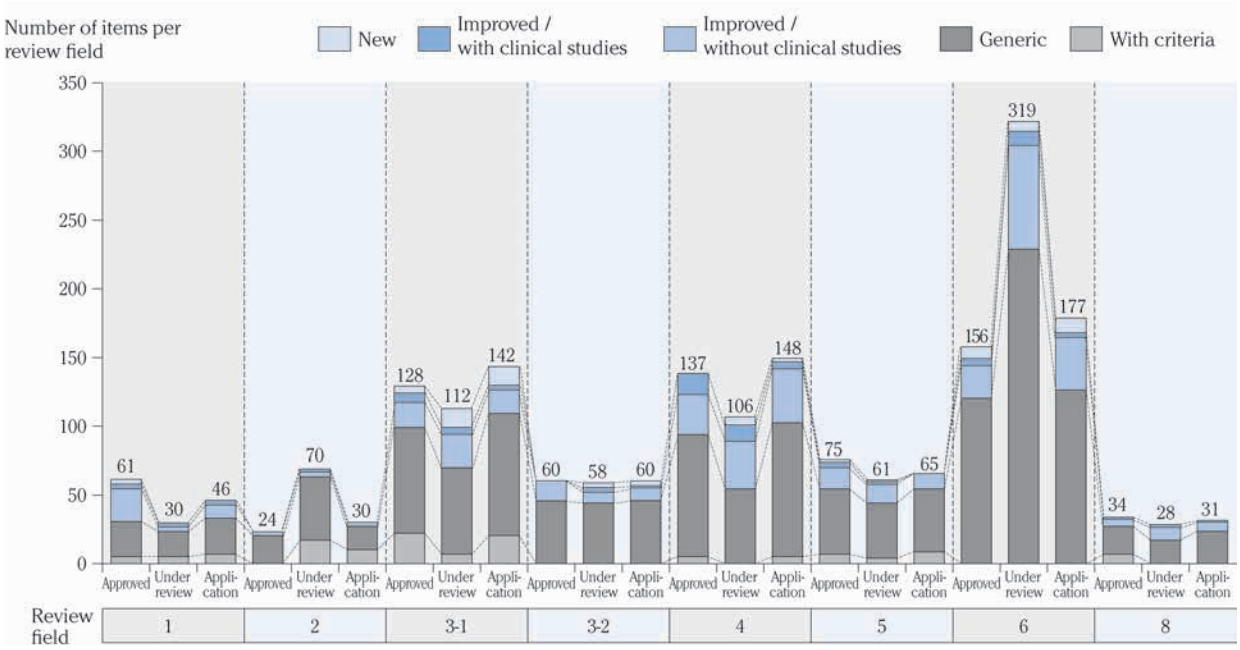


Figure 3. By review field: approval, under review, number of applications (as of December 31, 2011)

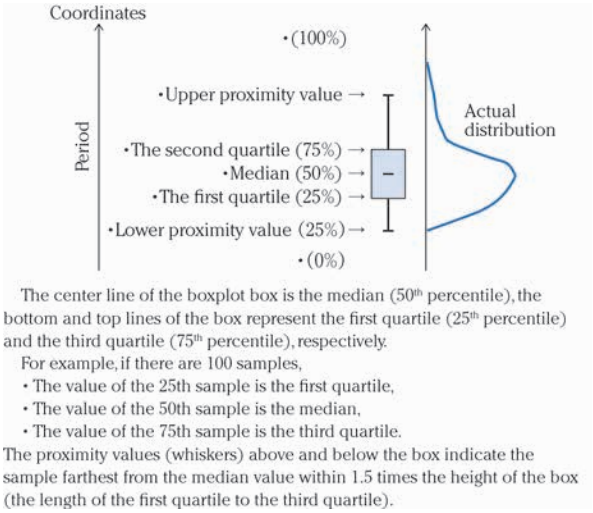


Figure 4. Description of Boxplot

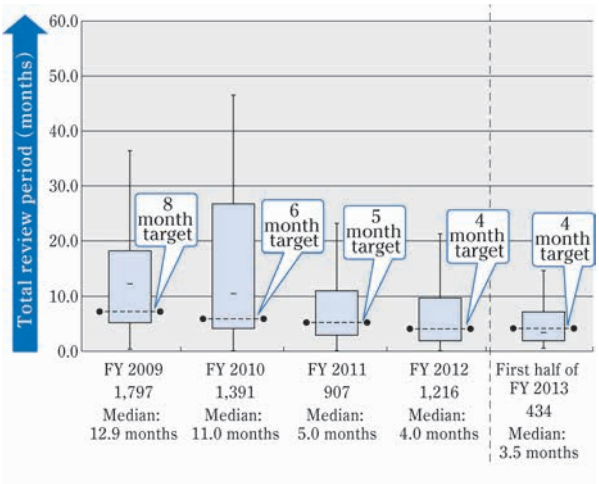


Figure 5. Generics approval distribution (total review period)

and the performance goals were switched to a percentile method and application cohort, as recommended in the 2008 Device Lag Survey. From April 1, 2019, the third round of the Collaboration Plan for Optimizing Medical Device Regulations and Reviews (FY2019 - 2023) began. Time Clock monitoring continues and efforts will be made on the new theme of optimization of regulations and reviews.

7. From Conflict to Dialogue

Thanks to the Action Program, relationships between government and medical device organizations, and relationships between the PMDA and applicants dramatically improved. The device lag between Japan and the US has been significantly shortened (Comparison with Europe is not made as their system is different.). In some instances, products are approved faster in Japan.

What were the success factors of the Action Program?

1) The performance goal was to shorten the total review period, and both government and the industry shared responsibilities. The AMDD worked to fulfill its own responsibilities while putting forth requests.
2) Discussions were based on objective data. In particular, counter-data independently collected by industry groups were available.
3) The US review system was introduced. This was made possible by the effort of AMDD's RAQA committee members, and largely attributed to the contributions of Phil Agress of the AdvaMed, who provided much information about the US FDA review system, and the great achievements of Susumu Nozawa, who was based in the US (BD at that time) and joined the RAQA Committee.
4) The presence of the MHLW, who acted as a buffer.
5) US governmental support. Once every six months, we were contacted by the US Embassy to report on the

Contribution

What I have Witnessed in 10 Years of the AMDD

Isao Tanabe, Medical Journalist

Grateful for the past and hopeful for the future

Congratulations to the AMDD on the 10th anniversary. I revisited the website and recalled the era of the predecessor of the AMDD, the ACCJ Medical Device and IVD Subcommittee (hereinafter "Subcommittee").

As an Asahi Shimbun reporter, my focus was on new technologies and treatments that help patients. Many of the new treatments are attributed to imaging devices and review methods rather than drugs. However, many Japanese device manufacturers are small businesses, and most of them refused interviews, saying that publicity is not supported by the MHLW. Around that time, I learned of the Subcommittee, which had the latest device information from the US, and was willing to disseminate the information to patients. The Subcommittee provided us media with technical information on new devices from 2002.

In October 2004, I acted as the moderator in a general symposium, Toward Patient-Centered Medical Care, held by the Subcommittee. The speakers; Dr. Yasuhisa Sakurai, Professor Emeritus of Tokyo Women's Medical University, and Susumu Hidaka, Vice Chairman of the Japan Association of Cardiac Pacemaker Friends, have since passed away. And Takako Watt of the Breast Cancer Network Japan ("Akebono-no-kai") has retired from her 40-year-tenure as Chairman. I feel the passing of time.

Thanks to the Subcommittee and the AMDD, we were able to discover and learn about the latest treatments. They talked about not only minimally invasive devices and technologies that they wanted to sell, but also serious issues including patient quality of life, prevention of infection and maintenance inspections, and medical economy. I assume that it was because the public and patients needed to understand healthcare correctly in the West. I think that these activities changed public knowledge in various ways, and led to speedier resolution of device lag problem.

I'm retired now but I still go to New Year parties, and I am so happy to see old faces there. I find it very Western when I see not only the former government officials but also former workers in companies are now working for their rivals.

It is strange but in Japan, there have been a tug of war going on, bypassing the patients, between the manufacturers who want to raise prices and the healthcare professionals who pay for the products and wish to lower prices. However, with an aging population and spiraling medical costs, the survival of the medical insurance system is in jeopardy. To continue a system beneficial for the medical product buyers, patients, and healthcare professionals, it is imperative that we address wasteful medical practices, excessive medication and tests, and high-priced medical care disrelated to costs. These are the times when the wisdom and leadership of the AMDD are once again put to the test.

(Former Asahi Shimbun Staff Writer)

progress to the Director of the International Trade Administration's Office of Japan from the US government.

It's not our intention to refer frequently to the US but we cannot deny the fact that we learned a lot from them. Our major success factor was that we were able to take full advantage of the strengths of the US business association.

As a result, we were able to, albeit gradually, create the strong relationship we have now. We were rewarded when the PMDA requested us to provide training for new employees, as the PMDA had been adamant about not relying on the industry. We were able to work together on the inspection and training at AMDD member-company manufacturing facilities and their training facilities. As those opportunities increased, the PMDA was able to gain a deeper understanding of the products and know-how needed for reviews.

Now the PMDA has become an Asian leader and the PMDA of the world. The PMDA's philosophy, which translates as: "We strive to be a bridge of hope for patients by delivering more effective and safer medicines and medical devices to medical sites faster," is also our mission at the AMDD.

We would like to pay tribute to the PMDA for achieving "reform close to a revolution" and to Dr. Tatsuya Kondo, its former Director who led those reforms.

Reference

1) ACCJ Medical Device and IVD Subcommittee: "2008 Device Lag Survey: Supporting Governmental Initiatives to Accelerate Reviews (October 2008)"
2) MHLW: Medical Device Review Acceleration Action Program, December 11, 2008
3) Junko Kodama: "Medical Device Review Acceleration Action Program: The Outlook from the Turning Point: 2011 Time Clock Survey", Pharmaceuticals and Medical Device Regulatory Science. 2011, 42 (7). P.573-9.
4) Junko Kodama: "Medical Device Review Acceleration Action Program: 3rd Year Validation", Pharmaceuticals and Medical Device Regulatory Science. 2012, 43 (9). P.811-22.
5) Junko Kodama: "Medical Device Review Acceleration Action Program: Final Year Validation and New Collaboration Plan", Pharmaceuticals and Medical Device Regulatory Science. 2014, 45 (4). P.306-21.

Orthopedic Surgery (Artificial Joints)

History of artificial joints and the current status

Artificial joint replacements has evolved by the development of implants during the past 50 years. Improved materials have extended durability exponentially, which is directly linked to long-term results, and improved design has been reviewed to reproduce function close to human biology. The surgical procedure continues to evolve dramatically, including patient-friendly minimally invasive surgical techniques, effective approaches to early recovery, and currently robot-assisted improved precision.

With these developments, the evaluation of artificial joint replacement has moved from the search for simple long-term results to the evaluation of their range of motion, and to patient satisfaction today.

It is no exaggeration to say that the current artificial joint replacements are expected to provide stable long-term results for joint diseases such as osteoarthritis and rheumatoid arthritis.

These developments in artificial joint replacement have shortened the length of hospital stay and accelerated recovery, resulting in higher patient satisfaction. The number of cases, even with knee conditions alone, has doubled in Japan over the past decade; however, its prevalence rate is far lower than that in other countries, which is not well known. Westerners who value an active life choose artificial knee joints at an early stage if they experience strong pain and X-rays confirm a decrease in the cartilage tissue around the knee joints. In Japan, the number of hip replacement procedures are only 1/4 of the average in OECD countries, and knee replacements, only 1/2. In particular, when compared to the countries with the highest number of cases, the number of hip joint replacements are 1/7 or less and knee joints, 1/4 or less in Japan.

The importance of maintaining mobility in aging societies

Japanese have one of the top life expectancies in the world. However, the bones and joints are not able to cope with the longer life-span. The main cause of long-term care is stroke for the pre-elderly (65 to 74 years old), and is motive organ disorder, including debility due to aging, fractures and falls, and joint diseases, for the very elderly (older than 75 years of age). Furthermore, motive organ disorder is not only a causative disease for support or long-term care, but also a risk factor for indirect dementia and long-term care that hampers social participation. Arthrosis affecting motor system, particularly joint function, is directly linked to healthy life expectancy. For arthrosis of the knee alone, there are already 10 million patients with painful joints. The number of potential patients is said to be about 30 million. Early intervention can reduce medical costs and realize improved QOL and prolong healthy lifespans.

In this way, orthopedic medical devices contribute significantly to extend healthy life expectancy. If patients receive appropriate diagnosis and treatment options, they can have the opportunity to take an effective course of action at an early stage, including surgery before the bones and joints weaken. This can reduce the risk factors of indirect dementia and long-term care that hampers social participation.

To realize this, for example, diagnosis of joint function (beyond patient inquiry / X-rays) can be added to health check-ups. Then, the risk of developing arthrosis can be identified at an early stage to pave a way for an appropriate treatment intervention.

Economic background

The economic impact of undermining healthy life expectancy is enormous. It has been suggested that knee joint damage has a major impact on a country's economy. A study by the American Academy of Orthopaedic Surgeons concluded that artificial knee joint replacement can save approximately 40,000 dollars in medical treatment costs, which brings the social benefit between 10,000 to 30,000 dollars[1]. According to the economists' survey, hip replacements in Japan can reduce eventual medical costs by more than 2.9 million yen[2]. Research on direct and indirect costs for the treatment of end-stage knee osteoarthritis found that total knee replacement (or total knee arthroplasty (TKA)) is a very effective operation, and 90% of patients reported that they are pain-free, return to work, and have a significantly improved standard of living. The research also reveals that bone and joint disorders account for a number of workdays lost for 440 million workers per year, surpassing any other medical condition[3].

However, many of the joint conditions are chronic, progress relatively slow, and they are overlooked and viewed as part of the aging process. Restoration of worn-out joint cartilage to its original condition is difficult and such cartilage gradually deteriorates with age. If patients put up with pain over many years and postpone treatment, sarcopenia may develop. Then the innate mobility is undermined; loss in terms of social contribution is extremely large.

Approximately 3.5 million workers are taking care of their families, and every year over 100,000 of them leave their jobs to give care and nursing. Reducing the risk of dementia and long-term care can result in mitigating the risk to patients, their families, and people around them in regard to their social participation and economic activities.

Improving in-depth knowledge of the general public on knee and hip joints is an important agenda in a super-aging Japanese society. Information overload, a harmful effect of today's information society, makes it difficult to select reliable information. Against this backdrop, the AMDD's Orthopedic Committee has a duty to actively improve correct healthcare literacy for citizens, together with local governments and medical institutions.

Reference

1) http://newsroom.aaos.org/media-resources/Press-releases/benefit-sofkneereplacement.htm#rel
2) https://www.advamed.org/sites/default/files/resource/eiu_study_final_japanese.pdf
3) Burden of Musculoskeletal Disease, U.S. Bone and Joint Initiative, 2011

Orthopedic Surgery (Spine)

In recent years, the outcome evaluations and healthy life expectancy that are discussed in the context of medical administration, are strongly related to lifestyle-related diseases and medical disorders. Meanwhile, no matter how healthy the internal body is, if the musculoskeletal function supporting it is not in good condition, a patient is not truly in good physical health. Looking at the future social structure of Japan, it is very important that people stay active suitable to their age and lifestyle. Daily activities such as walking, standing straight, sitting on a bed or wheelchair, swallowing and breathing without problems are all deeply related to the vertebra (spine). To achieve true quality of life, the spine literally functions as a backbone.

To deliver optimal and safe treatment for patients with spinal disorders, the spinal surgery field, and the medical devices and systems for such use, have evolved significantly over the past decade. The following three innovations are introduced:

1. Innovation for minimally invasive surgery

Traditionally, it was necessary to approach spinal surgery with a large incision and opening up of skin and muscle (Figure 1). However, with the development of minimally invasive surgery that reduces damage to the body, the development and improvement of medical devices for such surgery are now in their advanced stage. Typical examples are a discectomy of a lumbar disc herniation under endoscopy and microscopy, percutaneous pedicle screw fixation using a cylindrical surgical instrument (Figure 2), and percutaneous vertebroplasty that performs percutaneously balloon dilation and cement injection for spinal compression fractures. These minimally invasive surgical procedures significantly reduce operation times and blood loss, contributing to shortened post-operative hospital stays. Medical device manufacturers are shifting their efforts from simply selling the products to the industry-government-academia initiatives to offering training for introducing new technology and calling for safety in cooperation with academic societies and the PMDA.

2. Innovations for improving surgical safety

As surgery has become less invasive and the patient population undergoing spinal surgery continues to expand, improvement of safety has become increasingly more important. In order to achieve more accurate surgery, navigation systems assisted by computer technology are gaining ground. Based on image data taken before surgery with an X-ray fluoroscopic apparatus, a 3D simulation is performed to determine the insertion position and angle of spinal screws. Benefits during surgery include accurate surgical operations by overlapping the operation site with a planning image displayed on a monitor, and lower radiation exposure to both the patient and physician due to reduced use of fluoroscopy. In order to mitigate the post-operative risk of nerve paralysis, a nerve monitoring device was developed to observe changes in neurological symptoms during surgery. Devices and software aimed at improving the safety of spinal surgery continue to advance.

3. Innovation for maximizing clinical outcomes

Innovations for maximizing clinical outcomes obtained from spinal surgery derive from the products and from evidence-building. Examples derived from products include vertebral cages that are surface-treated with titanium for better fusion with patients' bones, cervical artificial vertebra discs that preserve cervical spine mobility, and new bone grafting materials (human demineralized bone matrices) with osteoinductive characteristics. Examples derived from evidence-building include a surgical database in the form of a registry, which the Neurospinal Society of Japan and the Japanese Spinal Instrumentation Society are working on. These efforts of collecting big data in the spinal field facilitate Japanese evidence-building and global transmission of the information.

Innovation in the field of spine surgery outlined above will contribute to preventing people from becoming bedridden, an urgent issue for Japan, and to the shift from hospitalization to home care and nursing. Comprehensive innovation in the spinal field that combines hardware including medical devices, and software including education, evidence-building, and patient awareness, are indispensable for healthy Japanese life expectancy.

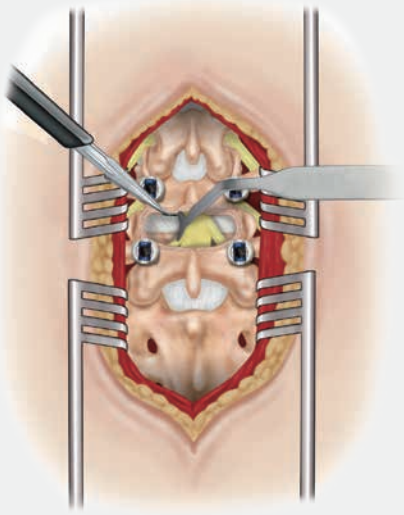


Figure 1

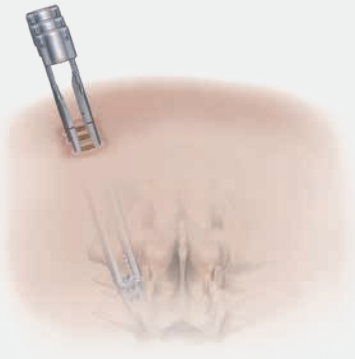


Figure 2

Round-table discussion

Central Social Insurance Medical Council (Chuikyo) Discussion

Chuikyo and 10 Years of the AMDD and Beyond, as Told by Successive Expert Members

Attendees (in order of term of office)

Mitsuo Hirose (1999-2005), Maverick Group representative, former President of Johnson & Johnson K.K.
Akira Matsumoto (2005-2011), Director at Rizap Group, former President of Johnson & Johnson K.K.
Makoto Tamura (2011-2017), Head of AMDD Medical Technology Policy and Research Institute, former Vice President of Abbott Japan Co., Ltd.
Tamotsu Hiiro (2017-2018), President and CEO of McDonald's Japan, former President of Johnson & Johnson K.K.
Toshifumi Hayashi (2018-present), Director of the Government Affairs at Edwards Lifesciences Ltd.

Kosuke Kato, AMDD Chairman, President of Edwards Lifesciences Ltd.
Junko Kodama (Moderator), Chair of AMDD Public Awareness Committee, Senior Director of Public Affairs at Edwards Lifesciences Ltd.

(Titles are as of the time of the roundtable discussion)

The expert members of the Special Committee on Medical Materials under the Central Social Insurance Medical Council (Chuikyo) are representatives of member companies of the AMDD or its predecessor, the ACCJ, who have been delegated by the MHLW. They have expressed their frank opinions concerning medical fees and other issues from the viewpoint of the medical devices and in-vitro diagnostics (IVD) industry.
Here, we look back discussions at Chuikyo over the past 20 years with five former and incumbent expert members, and asked them to talk about the achievements and difficulties within the industry, together with a few anecdotes.

The decades before and after Chuikyo participation

Kodama (Moderator): I am excited to see here former and incumbent expert members of Chuikyo. Thank you all for coming today.

Kato (Chairman): I would appreciate it if we could discuss how we struggled to bring good medical devices to Japan, and if we could talk freely along those lines.

Hirose: Yes, that's the backbone. That is the reason that I wanted to create the predecessor to the AMDD. In those days, even if you joined a Japanese organization to request something to the government, the Japanese organization didn't understand about foreign manufacturers and avoided you like the plague. So, it was only a matter of time before we decided to create our own organization. The ACCJ Medical Device and IVD Subcommittee (hereinafter, the Subcommittee), the predecessor to the AMDD, was created within the ACCJ by three individuals; myself, 3M Medical's Sam Narbon, and Becton Dickinson's Mark Thorndal.

Kodama: Hirose-san, you belonged to the Subcommittee, but what led you to become an expert member at Chuikyo? According to our records, you've been an expert member since 1999.

Hirose: Since around 1997, we had been frankly expressing what we wanted. Then the MHLW was suggesting it would be better to include a foreign representative. When I told them to consider foreign-affiliated companies more, they asked me to join.

Kodama: So after asserting yourself, you got a seat. That's how it started, isn't it?

Hirose: You have to keep asserting, even if they dislike you for it. Eventually, they'll listen to you.

Hiiro: So the expert membership started around your time?

Hirose: Yes, I was the first.

Hiiro: I thought so. Was there a medical device expert group before that?

Hirose: There was a materials committee.

Hiiro: Who was the representative?

Hirose: The one perceived to be the head of the materials committee was Kenichi Matsumoto, the President of Sakura Seiki. One thing we were grateful for was that Kenichi Matsumoto, who spent half his time in the US on business, was a veteran and always there to put in a word for us in Japan when we consulted with him.

Kodama: How were things at the Chuikyo at that time? I heard you were bombarded with questions at the start.

Mitsuo Hirose

Hirose: The Japan Medical Association was most opposed.

Matsumoto: There were differences in the arguments of Chuikyo and that of the AMDD. Basically, Chuikyo is the place to discuss money, most importantly medical fees, then naturally drugs. Materials came last. We weren't a major player. However, back then, in the latter half of Hirose-san's tenure, I remember various issues surfaced.

Kodama: Yes, let me just go through those issues. Foreign Average Price (FAP) was introduced in 2002, during Hirose-san's term. Prior to that, because of the Prefectural Purchase Price System, medical devices were given late approval although their prices were freely set by the manufacturer. In 2000, the Prefectural Purchase Price System was abolished.

In Matsumoto-san's term, the phrase "innovation evaluation" started to be heard, and in 2012 during Tamura-san's term, Australia was added to the FAP. A new evaluation rule was set up for accelerated introduction of insurance. Those days were marked by volatile exchange rates, and the establishment of the Special Committee on Cost-Effectiveness Evaluation under Chuikyo in 2012.

Owing to the prevailing view within the AMDD that the insurance system would not work, a value-based health care project was launched which led to a C1 challenge in Hiiro-san's term. Along with the C1 challenge application (a mechanism that allows the reimbursement application as C1 for those products whose safety, effectiveness, and medical economics are verified based on post-marketing clinical and non-clinical data), B3 (time-limited improvement premium) came along, though from the government. Then, in 2016, during Hiiro-san's term, a trial of cost-effective analysis began. In each term, there were big challenges. Can you all give us your opinions on them?

Medical device innovation and device lag

Matsumoto: After the Plaza Accord on September 22, 1985, the exchange rate at the time of 240 yen to the US dollar fell to 150 yen in one year due to the appreciation of the yen. For foreign companies in Japan, the price was cheaper because they were importing products. Another thing was the innovation, that started around 1990. If you compare medical devices from around 1980 with those around 1990 and 2000, they are completely different.

Hirose: That's very true.

Matsumoto: Innovations over the last 30 years changed most of healthcare to become minimally invasive one. However, the biggest problem Japan was facing in those days was the economic downturn, especially after the end of the Cold War in 1990, and rising medical expenses. This prompted the necessity to reduce the length of hospital stays. The most effective way is to make medical treatments minimally invasive. So most innovations have been based on minimally invasiveness.

I remember, laparoscopy started in 1989; now, laparoscopy is mainstream, with more than half of all operations being conducted laparoscopically. And intervention began in the mid-1980s at first it was the balloon, but during Hirose-san's term, we saw the arrival of the Palmaz-Schatz stent (Japan's first coronary artery stent). Following that, Cypher gained tremendous popularity. That's a drug-eluting stent, which is a stent coated with a drug to prevent restenosis of the coronary artery. Then we saw the arrival of the robot, da Vinci. So to be honest, my term was most eventful; the appreciation of the yen and the development of innovations continued. The market significantly expanded in that era, from 1990 to around 2000.

Hirose: Yes, that was when the market was booming.

Matsumoto: So the real problem during my time at Chuikyo was device lag. Even though new products were developed, Japan was slow to give them approval. In a similar sense, a device gap was also an issue.

Akira Matsumoto

However, those circumstances didn't stop the march of innovation, which contributed to patients and manufacturers, especially foreign manufacturers that enjoyed tremendous growth. Then, a slowdown of innovation followed. The device lag was almost resolved. But, the ensuing economic downturn in Japan increased burden on social security and price issues were hardly solved.

Kodama: Tamura-san, tell us about your term, which came after the very lucky and blessed term of Matsumoto-san.

Tamura: During my time at Chuikyo, there were specific debates on what to do with innovation evaluation. I joined the ACCJ Subcommittee in 2004, and six months later I became Chairman of the insurance committee. I was told in 2005 that the drastic relief measures in repricing would be tightened. So Matsumoto-san, who was with Chuikyo at the time, told them on my behalf that if that happened we would be squeezed. A physician in Group 2 was infuriated, yelling that it was out of the question especially since people in Japan regard the price differences between Japan and overseas as a big issue. I really felt that Chuikyo was a scary place. When the meeting was over, Matsumoto-san said to me in an easy-going manner, "That was tough, but they are just making a big fuss about it."

In the end the government agencies didn't squeeze things that much. Just a soft squeeze. But recently, medicine is being squeezed a little too much, making things difficult. In Hirose-san's time, things were tough at Chuikyo, though in Matsumoto-san's era, things got easier probably due to Matsumoto-san's skilled way of dealing with things.

Hirose: It's true. Their attitude was completely different. In my case, physicians in Group 2 just told me all I did was sophistry. You had to fight in those days. With a little advancement of innovation later on, things began to change, especially in the case of stents and minimal invasive procedures. Physicians then had to learn new technology. When Matsumoto-san was President of J&J, he focused on training and invested heavily in it.

The good thing about working with devices is that unlike pharmaceuticals, there is training before the sale, and assistance after the sale. Physicians come to the manufacturing company to receive training and that's why they come to know the hard work on our part.

Kodama: Yes, that is the big difference between medical devices and pharmaceuticals. The ACCJ has always appealed through the AMDD that medical devices are different from pharmaceuticals. Do you have any

opinions on that?

Hiiro: Well, just as Hirose-san said, when I went to the medical associations and spoke to physicians in Group 2, I always told them that pharmaceuticals were different from medical devices and that medical devices came with technology and had a learning curve. When I was there, there were discussions about cost effectiveness, so I asked them to not evaluate the devices merely as objects and to remember that the technology is an integral part of them. That is the characteristic that sets them apart.

Kodama: Did that understanding deepen within Chuikyo?

Hiiro: I would say that Chuikyo was the place for debates in the times of Hirose-san and Matsumoto-san, while in my and Tamura-san's time groundwork was laid outside of Chuikyo at meetings called "Hiraba" (level ground). During "Hiraba" meetings, we bargained with a view to form consensus rather than debating. As Matsumoto-san said, medical devices were last on the list; medical fees, drug prices, and then medical devices. As such, public interest was not so high. I didn't mention it much during "Hiraba", but I strived to send our messages outside Chuikyo.

In fact, we asked the Group 1 (payer) members to come over to our Tokyo Science Center. We showed them a tremendous number of orthopedic instruments and explained that they are lent and returned. Also, we actually demonstrated physicians' training. These experiences eventually made them grasp that the technology and products are inseparable.

Matsumoto: As long as we had a fair argument, no intense rebuttal would come. So, we felt there was nothing we could do but to correctly say the right things. Every company pursues the profit, but what's different about the healthcare business is that their priority is the patients. Next comes the healthcare workers. Training was really for physicians to learn the correct way to use the devices.

Kodama: It boils down to our wholehearted purpose to ensure that physicians use the devices safely on the patients.

Matsumoto: We know our devices better than anyone else. Therefore, I gave thorough training for our employees.

Tamura: I was reminded how important Chuikyo was in 2009 when there was a change in government and the Democratic Party of Japan became the ruling party, and Chuikyo didn't hold a meeting for a month. The Democratic Party that took power in September wanted to make big changes to Chuikyo. In October, despite being

Makoto Tamura

immediately before the revision, Chuikyo didn't hold a meeting. In mid-November, Chuikyo finally resumed operations. As an industry group, I was very worried about a possibility of decisions being made by somewhere else, so I escalated my concern to the Insurance Bureau, begging for the resumption of Chuikyo. Although I've been counter-attacked for my opinions expressed during "Hiraba" meetings, if you don't assert your opinions on that field, the checking system won't work.

Hiiro: The assertion was rather for warning than for discussion.

Matsumoto: Everything is recorded at Chuikyo. Everything you say is jotted down. So I wrote everything down in polite terms before speaking at Chuikyo.

Tamura: It's a bit technical but when we debated about transfer prices, Matsumoto-san explained it really well, and those members on the payer side agreed with his point, keeping us on the right track.

Matsumoto: What was particularly good in my term was support from those on the medical side, as I had quite a few medical professional acquaintances. Dr. Takamasa Kayama made some radical remarks, but when I explained well, he understood. You know I resigned as President of J&J and created an association to increase surgeons (NPO: The Committee to Encourage New Surgeons). Even at that time, if it were not for Chuikyo, medical fees would not have increased. For companies affiliated with the AMDD, the material price was a very serious issue, but medical fees were more important. If medical fees drastically decrease, drug and material prices will be affected. So in a sense, logical explanation can convince both Group 1 and Group 2. During my tenure, surgeon fees increased by 30 - 50%. That was when Akira Nagatsuma was the Minister for Health, Labor and Welfare in the Democratic Party Administration.

Hiiro: The estimation method of Gaihoren (Japanese Health Insurance Federation for Surgery) was very good.

Tamotsu Hiiro

Debate of in-vitro diagnostics (IVD)

Hayashi: By the way, diagnostics are part of AMDD's portfolio. When Tamura-san was an expert member, he said he'd like to express opinions on IVD at Chuikyo. This made it possible to input IVD in the framework within the materials section.

Hirose: At the beginning of the ACCJ era, diagnostics were not included.

Kodama: Is that so?

Hirose: A company called Ortho-Clinical Diagnostics (OCD), a subsidiary of J&J, had paired devices and diagnostics. The headache for them was that they had to file approval application for reagents as pharmaceuticals and devices as devices. So IVD was added in the ACCJ era. And the name was changed to ACCJ Medical Device and IVD Subcommittee.

Hiiro: I joined the ACCJ Medical Device and IVD Subcommittee and formed a consortium.

Tamura: The Japanese Promotion Council for Laboratory Testing.

Hiiro: Tadashi Suzuki and Kunikazu Teraoka from the OCD were involved in the establishment of the consortium. It was truly groundbreaking in that the consortium incorporated academia including the Japanese Society of Laboratory Medicine and the Japan Registered Clinical Laboratories Association that include the SRL and the BML to which tests were outsourced. If you made a proposal through the consortium, they (MHLW) listened to you. As a result, the downward revisions of medical fees for tests stopped. Similarly, a consortium with academia was created for large-scale medical devices, and then, medical fees increased.

Kodama: Staying silent doesn't help after all.

Hiiro: We learned that it's better to include academia in addition to the industry to facilitate talks with the MHLW.

Tamura: Since tests and large-scale devices involve technical fees, it was difficult to engage the materials committee in the process. Large-scale devices joined Chuikyo around 2008, but IVD officially joined in 2016. Half of the cases that passed C1 and C2 over the past year were technical fee inclusive. The ratio of STM is decreasing.

Going forward, medical device programs and digital items for the most part will be technical fee inclusive, so I think the big issue for the AMDD and Chuikyo is how to deal with that.

Hiiro: Yes, that's very important.

Technical fee inclusive or by function?

Matsumoto: Although it's not written anywhere, technical fees basically don't decrease. They may increase on occasion. There is no logic that material fees increase. Therefore, the technical fee evaluations are not necessarily bad even if recent cases are subject to technical fee evaluation after applying for C1 / C2.

Kodama: You have changed. You used to say no to technical fee inclusive, didn't you?

Matsumoto: Frankly speaking, I have changed.

Hirose: Now they say technical fee inclusive is getting better.

Matsumoto: Going back to 1998 during Hirose-san's tenure. Hirose-san made sutures technical fee inclusive.

Hayashi: It was 1996.

Matsumoto: It wasn't good to make it technical fee inclusive at that time. Though, it's better that way now.

Tamura: There are discussions as to whether technical fee inclusive is good or STM is good, but in fact there are many materials that don't fall into STM but only fall into the technical fee inclusive option. However, because the rules for inclusiveness are not so clear, I think a little more predictability is needed.

Hiiro: I think technical fee discussion as to whether technical fee inclusive or STM is increasingly important. It boils down to a discussion of what to do with the functional category. Some prefer category by brands,

Toshifumi Hayashi

and others prefer category by function. Realistically, considering the number of medical devices, it would be difficult to classify by brand.

Going forward, there will be cost-effectiveness evaluation, with ever more complicated FAP, it may be better to leave the current functional category as it is. Or I personally think that while making certain things technical fee inclusive, the industry must steer toward the direction of innovation evaluated in more highly fragmented functional categories. However, no consensus has been reached and it's going to be difficult.

On the premise that technical fees and the evaluation of medical materials are inseparable, what the industry wants to do with the system of functional category over the next 5 to 10 years will be very important. I think that the industry must debate this based on Hirose-san's and Matsumoto-san's past experiences and what they have learned.

Tamura: The functional category now has a special case, and now we have B3, so functional category is gradually changing.

Hiiro: At the time of the most recent revision when I was an expert member, that was a much debated topic. Medical devices are improved as we fine-tune it along the way, and this fine tuning process has been recognized to date to some extent. But from the standpoint of those who made the functional category, they don't welcome the request for premiums for such minor improvement. But we say that incremental innovation is important for medical devices, and it's unlikely that something like Opdivo becomes suddenly available. We negotiated how to make them evaluate incremental innovation. So at this time, there was a trade-off; the replacement addition (B3) was introduced while C1 challenge application was available.

At Chuikyo, I showed them an old pacemaker and the current leadless pacemaker, and explained that it wasn't a giant leap from the old to the new but rather incremental improvement that led to gradual miniaturization.

Matsumoto: The miniaturization and the price are two different stories. Innovation is advancing, but costs are basically going down. So it's unreasonable to ask to raise the price. It is needless to say that for the top management at every company prioritizes the interest of their own company, but egotistically arguing for their own interests gets them nowhere. So in a sense you have no choice but to take the greatest common denominator. Then, when a decision is made, some may suffer a loss, but overall that will not be the case.

Kodama: The AMDD also have prepared to take a hit and started a value-based healthcare project.

Matsumoto: On the other hand, there may be too much price erosion, depending on the product. This will kill us all, and will be a particular blow to the hospitals.

Hirose: Product creation with an aim to reduce hospital costs is now underway. If hospital costs are down, one physician can do the work of six to seven physicians because the rest will be handled by AI medical devices. That kind of product creation is ongoing.

Tamura: That sort of effort is also in line with work-style reforms, but there is debate on whether medical fees should be lowered as costs are lowered due to less workload of the healthcare workers. If medical fees are lowered, we, the provider of technology, will be also affected. How to address this is going to be extremely important discussion in the future. When the MHLW officials came to the AMDD for a lecture the other day, we asked that question, and their answer was that it would be a fixed payment or value-based healthcare or that sort of direction.

What is important in the future debates with Chuikyo

Kodama: Now, how do we go about working with Chuikyo? Would you advise Hayashi-san, the newest member of Chuikyo?

Matsumoto: Superficial measures would go unheard. It's important not to lose sight of the bigger picture and keep on asserting what really matters. I served as a member at Chuikyo for 6 years, but I've never touched on anything other than bigger issues. I only talked about the fundamentals. In most cases such fundamental stuff went through. Sometimes I've had to lay the groundwork in advance.

Kodama: And we must continue that stance.

Matsumoto: We are not real estate agents or land speculators. Our work exists because of the presence of patients, so we must not forget the fundamentals.

Kosuke Kato

Kodama: Yes, if that fails to be communicated, no one listens to us.

Tamura: The Government credited us with proactive proposals of new ideas in value-based healthcare. And some are now realized. For pharmaceuticals, we made a balanced proposal of new drug innovation premium, and that was also very positive.

This isn't just the work of the expert members, but it's important to make positive and sensible proposals as an industry group. Some people will poke holes in what you suggest, but Hayashi-san should persevere on the "Hiraba" of Chuikyo.

Hiiro: It may be a bit technical, but I have two points to make. First, in the past, discussions on medical devices were limited to those precisely on devices, but these days the drug product movement is so rapid and cost-effectiveness of medical devices is also discussed along with pharmaceuticals. So, I think we must make medical device claims based on how the policy on pharmaceuticals works out, and how the technical fee debate mentioned earlier works out. So, as Matsumoto-san said, with the whole picture in mind, it is necessary to see how to position medical devices within it. In that sense I think the current committee members have a lot of work to do with a full knowledge of all of these things.

My second point is related to advocacy. They say, "Make friends before you need them." It's too late to start making friends when you need them. So making friends before you need them is very important. You must have a framework for discussion ready before something happens, which need to be discussed.

Kodama: Hirose-san, any advice for Hayashi-san?

Hirose: I think it's true that we scarcely see the advent of breakthrough technology in recent years. The less breakthrough technology, the weaker our position in Chuikyo becomes and so does the position of the industry. The base for drug research has changed. Initially it was based on chemical compounds, then on biologics, and now on genes. Since the base has changed, people in the industry also must change. Then we'll see new products coming about.

Kodama: So ultimately, the more AMDD member companies develop new products, the more their position is strengthened.

Tamura: The fields of structural heart diseases and neuromodulation are steadily but surely expanding.

Hirose: Autologous cell sheets regenerated from cells, and autologous knee cartilage in orthopedics were developed through the partnership of a machine manufacturer and a biotechnology company. Collaboration among sectors may significantly change the medical device field.

Kodama: We're now in an era where it is difficult for one company to complete the whole process.

Matsumoto: Many great products have been developed in 10, 15, 20 years prior to the last decade that was quite uneventful. For example, stents later evolved into drug-eluting stents. And laparoscopy came about.

Kodama: We also had transcatheter aortic valve implantation (TAVI).

Hayashi: The revisions over the past few years comprised of two parts; evaluation of innovation and financial issues. Listening to what's being said, the mechanism for evaluating innovation enabled a number of things. So, as an organization we need to clearly convey the value of innovative medical devices, to send out our messages what must be evaluated, and to make the message understood at Chuikyo. Even with smaller changes, there must be a value proposition for patients.

Hirose: That is what we must continue.

Matsumoto: Decades ago, the Premium for innovativeness was established, but has there been any other system in place since Cypher?

Hayashi: Nothing. The Premium for innovativeness was applied for Cypher for the first time, and that's it.

Matsumoto: That was 15 years ago in 2004.

Making more people understand medical devices and IVD is key to the future

Tamura: However, for very innovative products, the reimbursement price may be determined by the cost calculation method. Thus, we can't simply say that it is problematic if we do not have the Premium for innovativeness. Another thing I'd like to point out to Hayashi-san is that it's the government that makes the

final decisions after all, so it's extremely important to have someone in the government offices who is knowledgeable about medical devices.

For example, a medical officer had been in the medical division prior to moving to the economics division where he stayed until last year. He is concerned about medical devices. During his tenure in the medical and economics divisions, he was tough on us time to time, but his approach was balanced as he did a lot of positive things based on his deep understanding of medical devices. What's more, he held study groups for young people at the Japan Association for the Advancement of Medical Equipment (JAAME) when he was in Japan. Even after studying abroad, he regularly participates in the study groups by Skype. He tries to understand and support the medical device industry. I'd like to see more people like him.

Hirose: That's great. That's the kind of people we need.

Hayashi: During discussions at Chuikyo, I must speak carefully while considering advice from everyone. In the meantime, we deliver our message to stakeholders with the help of all our experienced predecessors. I suppose that is one of the goals for the AMDD.

Matsumoto: In my experience, payers were not necessarily trying to make everything cheaper, and medical professionals were not necessarily trying to raise only medical fees while reducing material costs. If things were explained properly, they understood. That's why, when the number of surgeons decreased and something needed to be done, I thought about devising a way to raise medical fees.

At that time, Dr. Kayama, Dr. Itsumi and I asked the President and the Vice President of the Gaihoren to make a statement for us at Chuikyo. It was a great statement. Afterwards they (including public labor committee members) said they didn't realize that things were so bad. Despite their busy schedule, the Gaihoren used the National Clinical Database (NCD) to classify surgery into A, B, C, D, and E depending on its level of difficulty. Medical fees were raised to 50% for E and 30% for D.

Junko Kodama

Even today, surgical medical fees are not that good, but much better than back then. Just because we are medical device manufacturers does not mean we should only consider medical device issues. We have to take the entire industry into consideration.

Kodama: And finally, Chairman Kato, could you give us your thoughts?

Kato: I don't know about Hirose-san's era, but Matsumoto-san used some interesting caricatures to impress Chuikyo. It was amazing. Tamura-san took a theoretical approach, while Hiiro-san was like a salesman, dealing with both Group 1 and Group 2 as his customers. So it remains to be seen how Hayashi-san will work to make further improvement on their legacies. I hope he can even outplay his predecessors.

As Hirose-san mentioned, the drug development stage is changing, and in recent years there's been no innovation in medical devices. Increased change means that the development stage may be also changing. AI isn't fully developed and it is not something you actually realize, hence the concept of STM is wearing thin. How to keep holding discussions on technical fee at the STM committee is a very important mission in a mid to long-term.

Hirose: Let's leave it there.

Kodama: I would like to thank all of you for taking time out of your day to participate in the discussion today.

(Recorded in Tokyo on April 17, 2019)

Cerebrovascular Disease

The third leading cause of death in Japan: Finding the answers to the treatment of cerebrovascular disease

Cerebrovascular disease (stroke) kills approximately 110,000 people each year, making it the third leading cause of death in Japan*.

* MHLW, 2017 demographic statistics (determinate number)

Stroke can be roughly divided into hemorrhagic cases including subarachnoid hemorrhage which is caused by rupture of the cerebral aneurysm, and ischemic cases causing cerebral infarction due to a thrombus. Both hemorrhagic and ischemic cases may cause paralysis, language disorder, and motor dysfunction, which results in long-term nursing care, becoming bedridden, or death.

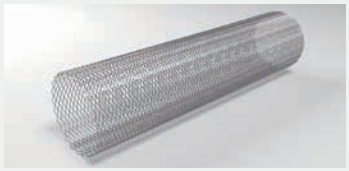
Minimally invasive advanced medical care has developed over the past decade. This contributes to reduced physical and mental burden for a wider range of stroke patients and improves their QOL after recovery.

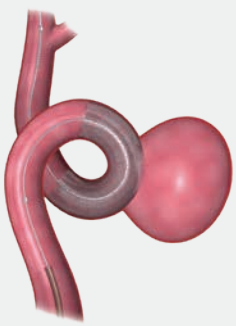
The age of post-platinum coils

The first treatment developed and introduced as a minimally invasive procedure for cerebrovascular disease was cerebral aneurysm coil embolization (endovascular treatment) that treats or prevents ruptured cerebral aneurysms. Unlike conventional craniotomy, endovascular treatment uses a catheter that is inserted into the blood vessel and guides a thin, soft spiral platinum coil to the cerebral aneurysm. This treatment fills the cerebral aneurysm with the coil to stop the blood inflow into the aneurysm and prevent bleeding from the rupture of aneurysm. This treatment introduced to Japan in 1997 became a forerunner of minimally invasive treatment.

However, performing coil embolization on an aneurysm which has a wide entrance (neck) was very difficult. To that end, adjunctive stents were introduced in Japan in 2008. Adjunctive stents were developed for the purpose of preventing protrusion or deviation of the coil mass from the parent artery during coil embolization, even when the aneurysm entrance is wide.

In 2015, flow diverters, the first stent-like device for treating cerebral aneurysms, were introduced in Japan. These devices made it possible to treat large and giant aneurysms (only for aneurysms with a maximum 10mm diameter and 4mm neck, and excluding rupture acute phase aneurysms), which had been defined as difficult-to-treat cerebral aneurysms. Such difficult-to-treat cases are as follows: even with treatment, blood flow into the cerebral aneurysm cannot be fully blocked, and hence cannot be completely cured; and re-treatments are necessary because measures to prevent cerebral aneurysm are not effective. Flow diversion is a new treatment method; while preserving the original blood flow of arteries, blocking the blood inflow to the cerebral aneurysm, proliferating endothelial cells at the neck of the blocked cerebral aneurysm to induce the formation of a new tunica intima, and reducing the risk of cerebral aneurysm ruptures. However, its placement is limited to sites from petrous part of internal carotid artery to the upper and lower petrous part, and the treatment is very difficult. Therefore, as of June 2019, the treatment with flow diverters is performed at limited facilities in Japan.





Flow diverters for cerebral aneurysm treatment

New treatment options for cerebral infarction

For acute cerebral infarction, which is the most common type of stroke, there are two therapies: internal therapy of intravenous t-PA treatment, and thrombus collection therapy which uses a thrombectomy device. Thrombectomy therapy was first introduced in Japan in 2008. Since then, we have seen a decade of innovation in thrombectomy. In general, acute cerebral infarction develops in the middle of the night or in the morning, and the onset timing is often not clear. The t-PA cannot be used in some cases because of the body constitution and treatment of other diseases.

In 2010, as a new treatment option for acute cerebral infarction, a soft, wire thrombectomy device with a spiral tip was launched for the first time in Japan. This enabled treatment of those patients who were unresponsive to t-PA (internal treatment) within 8 hours of the onset of acute cerebral infarction, or those who were not eligible for internal treatment. The results of clinical studies showed that 70% to 80% of occluded blood vessels are reopened with endovascular treatment for acute cerebral infarction using this device.

In 2011, approval was given to a device that collects thrombi while breaking them down with a catheter equipped with a powerful aspiration pump. Then in 2014, a stent-type thrombectomy device was introduced, and this improved reopening rate and safety.

In 2019, more than 10 years after the introduction of the first thrombectomy device, the indication of the device was expanded; treatment within 8 hours after the onset was expanded to treatment within 24 hours after the onset for some stent-type thrombectomy devices. This also allowed the expansion of treatment options to include those patients who might have suffered serious sequelae as they had not been eligible for this device, such as those with unknown onset times or those who presented with cerebral infarction symptoms upon arising in the morning.

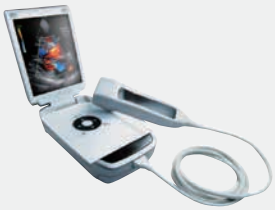
Thrombectomy devices for the treatment of acute cerebral infarction

The next 10 years

In the last 10 years, endovascular treatment for cerebrovascular disease has evolved and allowed patients to have more treatment options. According to Stroke Treatment Guidelines 2015 (Supplement 2017), it is highly recommended that patients diagnosed with acute cerebral infarction be treated with mechanical thrombectomy within 6 hours of the onset in addition to the conventional medical treatment (Grade A). Going forward, endovascular treatment is expected to become the standard treatment for an increasing number of patients.

Diagnostic Imaging

Products for diagnostic imaging use can be roughly categorized into X-ray equipment, CT, MRI, ultrasonic diagnostic equipment, and nuclear medicine equipment[1]. Among these, ultrasonic diagnostic equipment showed a dramatic improvement as pocket-sized devices were marketed in 2010. Thereafter, several improvements have been made. Taking this product as an example from the perspective of innovation in medical devices, we hereby discuss its significance.



Pocket-sized ultrasonic diagnostic equipment

Ultrasound diagnostic devices in the size of a conventional laptop have been available; however, the best feature of this product is its small size that can fit in a shirt pocket and can be operated intuitively with a single thumb. A probe is connected to the main body that has a 3.5-inch LCD panel. Since its launch, it has been presumed that the device is used in home medical care, emergency / disaster medical care, and remote medical care[2], and its usage scenes and users are expected to expand. Product feature is not limited to its compact size. One user comments its clear image and 20 seconds to start up as excellent features of the device[3]. The fast start-up time is one of the needs in emergency outpatient calls, where speed is everything. Apart from its size, the product feature factors in actual use in the medical field.

This product continues to be improved. In 2014, a 2-in-1 probe model was launched; the model has a probe at each end and can depict deep organs and superficial organs. With built-in probe that can depict superficial organs, visualization of superficial blood vessels, prostate, thyroid gland, and lung echo (pneumothorax) is possible[4].

2-in-1 probe (processed image)

The model eliminated the need to replace probes. This time-saving feature was useful for home care and emergency outpatient calls and disasters.

In 2017, a new model was launched. It realized operability similar to a smartphone, and was equipped with a touch screen function, a 5-inch LCD display, and a Wi-Fi function. The start-up time was further shortened to one second, addressing the need for a quick diagnosis in life-saving emergencies [5]. In a clinical setting where a user may need to perform breathing and circulation assessments in a short time (in emergencies), the user listens to the patient's chest with a stethoscope with the right hand, while starting the product with the left hand [6]. Further shortening of start-up times was prompted by such needs from users. Smartphone use was not spreading widely in 2010 when the first model became available, but in 2016, smartphone usage rate exceeded 70% [7]. With the incorporation of smartphone-level operability into the device at that time, users could use the device intuitively. This model had a built-in measurement application for residual urine volume. It had been in high demand in the primary care field where patients have no or fading sensation of residual urine. Residual urine volume can be measured semi-automatically [8]. These elements are also seen as improvements from the user's perspective.

Moreover, a new model launched in 2018 was equipped with new functions useful for diagnosis, and quantitative measurement and analysis applications. Output function to an external monitor allowed test images to be displayed on a large-screen, and patients, family members and medical staff can view the screen together. Function to create and register procedures for surgeons, and function to adjust images and assist various users were also added [9]. The improvements for usability of users were achieved this time using software.

At the time of the launch, the device attracted attention for its potential usage environments, enabled by its pocket size. As it turned out, various improvements continue to be made in order to keep reflecting the needs of users, suitable for their method and purpose of use other than the expected usage environments. "Innovation" is a status deemed where a new or improved technology has become prevalent. It is only after the technology is prevalent that it begins to contribute to the needs of medical sites, and is called innovation. Since its first launch in 2010, over 5,200 of the devices have been sold in Japan (as of April 2017) [10]. Going forward, we must continue to understand medical needs and play a role in innovation that underpins medical setting.

Reference

1) Trends in diagnostic imaging equipment in recent years, Special Feature Trends in medical equipment in recent years and electrical equipment 2, Academic Journal of the Institute of Electrical Installation Engineers of Japan, May 2005, Vol. 25 No. 5, P313 - 316
2) Nikkei Digital Health: https://tech.nikkeibp.co.jp/dm/article/NEWS/20100708/184067/?ST=health
3) RadFan ONLINE http://www.e-radfan.com/column/5150/
4) Nikkei Digital Health: https://tech.nikkeibp.co.jp/dm/article/NEWS/20140613/358380/?ST=health
5) Nikkei Digital Health: https://tech.nikkeibp.co.jp/dm/atcl/news/16/070608265/?ST=health
6) Users' Voice, Doctors' Voice http://gecommunity.on.arena.ne.jp/Vscan/dp/user.html
7) 2016 Survey on Information Communication Media Usage Time and Information Behavior <Summary>, July 2017, Ministry of Internal Affairs and Communications Policy Institute
8) CNET Japan: https://japan.cnet.com/release/30198832/
9) Nikkei Digital Health https://tech.nikkeibp.co.jp/dm/atcl/news/16/111611700/?ST=health
10) Website of manufacturer: http://www3.gehealthcare.co.jp/ja-jp/event_and_news/news_and_initiatives/2017/press05

Chapter
3

Cooperation and Collaboration with the MHLW and the PMDA that led to the Pharmaceuticals and Medical Devices Act

1. Introduction

Before the 10th anniversary of the American Medical Devices and Diagnostics Manufacturers' Association (hereinafter referred to as "AMDD"), there was a revision of the Pharmaceutical Affairs Law (PAL, now the Pharmaceuticals and Medical Devices Act). At the time of revision, the Regulatory Affairs and Quality Assurance Committee (hereinafter referred to as RAQA Committee) of the AMDD made active policy recommendations to the MHLW/PMDA, and carried out activities to achieve its recommendations.

2. From the Pharmaceutical Affairs Law to the Pharmaceuticals and Medical Devices Act

The PAL had been amended since it was enacted in 1960. However, the promulgation of the 2013 revision and the enforcement of the revision in 2014 were extremely important turning points.

The revision came at a time when the AMDD moved from action programs to collaborative plans, and AMDD pinned great expectations on the revision. The RAQA Committee Leadership Team compiled expectations in their proposals on the revision of the PAL for medical devices (including in-vitro diagnostics) titled, "Medical Device Regulation Issues in Japan and their Solutions" [1].

In accordance with the PAL then, the MHLW imposed various regulations in the approval review process of medical devices: design and development stages, approval application and review, approval by the Minister of the MHLW, and market launch. The issues at each stage were classified into seven areas (design / risk management, quality management system (QMS), software / IT, clinical studies, pre-marketing review, Good Vigilance Practice (GVP) and business category), as shown in **Figure 1**, and then analyzed.

The results of the analysis led to the recommendations summarized to the right.

Some issues have been resolved, and some are midway through their journey, but it is safe to say we are now steadily approaching the ideal status of the AMDD as recommended by the RAQA Committee back then.

Of particular note is the recommendation written in the proposal related to overall PAL, to divide the descriptions in

Recommendations concerning the revision of the Pharmaceutical Affairs Law for medical devices (including in-vitro diagnostic devices) [1]

Proposals for the Pharmaceutical Affairs Law as a whole

- Divide the descriptions of Articles in the Pharmaceutical Affairs Law into "pharmaceuticals, quasi-drugs, and cosmetics", and "medical devices"
- Apply the content of ISO 13485 without changing it

Proposals on individual matters

Article 1 of the Act (Objective)
- Add "Accelerated introduction" of medical devices and a viewpoint "to contribute to the health of the public."
- The term "efficacy" is associated with pharmaceuticals, and thus, it should be changed to "performance" for medical devices.

Article 12-2 of the Act (Permission Criteria)
- Integrate GVP / GQP because ensuring quality and safety are two sides of the same coin

Article 13 of the Act (Permission for Manufacturing)
Article 13-3 of the Act (Certification of Foreign Manufacturer)
- Regardless of domestic and overseas products, make QMS a requirement, and change the manufacturer's permission / certification to the registration system.

Article 14 of the Act (Manufacturing and Marketing Approval)
- Expand the current concept of "one item", and build a mechanism for obtaining approval and certification for each principle of the medical device.
- Likewise, instead of reviewing to "identify" devices as in pharmaceuticals, introduce an evaluation method with minimum necessary data from the design management (least burdensome approach)
- Replace "by item" QMS compliance inspection with appropriate maintenance and management of QMS (especially design management portion), to expand the unnecessary scope of a partial change application and to timely perform improvement.
- Abolish review other than GCP and GLP as it is redundant with QMS design management.

Article 23-2 of the Act (Certification of Manufacturing and Marketing Designated Controlled Medical Devices)
- Entrust the review of low-risk items (equivalent to general medical devices) to a registered third party certification body along with a QMS compliance inspection.

Article 63-2 of the Act (descriptions in package inserts, etc.)
- Introduce package insert system from the users' point of view (e.g. provision of electronic files on Internet, substitution by instruction manuals)

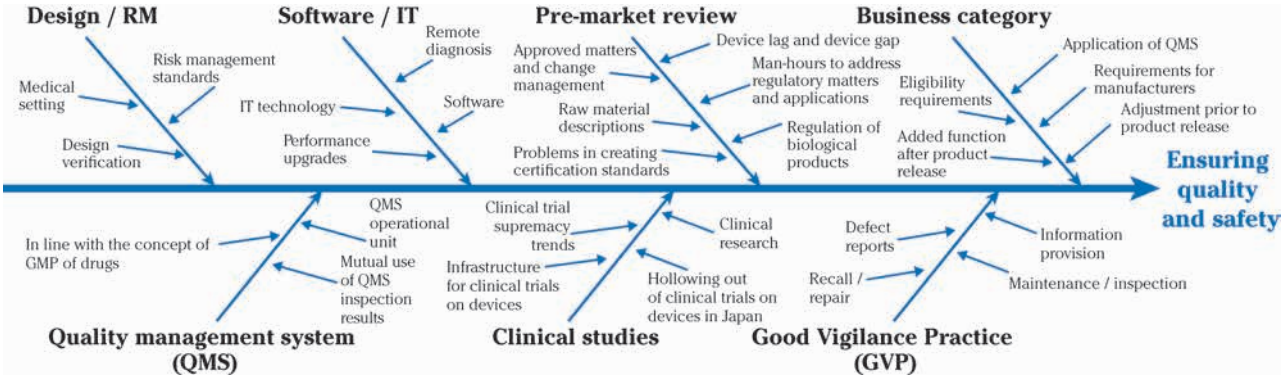


Figure 1. Analysis of issues on medical device regulation

each Article of PAL into "pharmaceuticals, quasi-drugs, and cosmetics", and "medical devices (including IVD)". This has been the long-held vision of the medical device industry since the time when medical devices were called medical tools.

Medical devices and pharmaceuticals are of completely different nature in the first place. Medical devices have evolved from tools used in treatment and diagnosis. They are designed and evaluated based on their purpose of use (development concept). With feedback obtained from healthcare professionals in the clinical setting, medical devices need to be placed in a continuous cycle of improvements.

This cycle has failed to operate because the regulations for pharmaceuticals (whose approval does not or should not change) were applied to medical devices (which must be continuously improved), and this was a part of the reason for the device lag.

The enactment of regulations suitable for the characteristics of medical devices, envisaged by the entire medical device industry including the AMDD, took a major step forward when the revision of PAL stipulated that medical devices be in a separate chapter. The name was also changed from the Pharmaceutical Affairs Law to "Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Pharmaceuticals and Medical Devices Act)".

This was a great result that the entire medical device industry has finally managed to achieve. For a long time, we have been trying to enlighten people about the differences between pharmaceuticals and medical devices at various venues. We owe a great deal to those at the MHLW and the PMDA who listened sincerely to the industry recommendations and worked towards the realization of our vision. We would like to take this opportunity to express our gratitude again. We also believe that the trusting relationship with the MHLW and the PMDA, cultivated through action programs and collaborative plans, has helped us press forward.

Moreover, the 2013 revision added regulations for single programs and regenerative medicine, and set the stage for the development of an area which did not exist in the past, and where regulations did not keep up with the speed of development.

With regards to IVD, a number of proposals and revision requests have been prepared and disseminated by a joint team of the IVD 3 groups (AMDD, JACRI, and EBC). Through this communication, awareness of industry issues is shared with the government. More than a few issues have been resolved or resolving through past and ongoing legal revisions and collaborative plans. The main recommendations are shown below.

- Position paper "Thoughts on the Handling of In-vitro Diagnostics", August 4, 2010
- "Proposal on Infrastructure Building for Companion Diagnostics for the Promotion of Personalized Medicine", October 21, 2011
- Legal Revision Request "Proposal for Revision to the Pharmaceutical Affairs Law for IVDs", July 20, 2011
- "Proposals on the Appropriate Provision of In-vitro Diagnostics" based on Diversifying Medical Needs, June 17, 2014
- Law Revision Request, "IVD Industry Request for a Revision of the PMD Act", July 5, 2018

In particular, the advent of companion diagnostics was a milestone in the IVD field in the past 10 years, as described in the article, "10 Years of Innovation Saving Patients" on page 36 of this journal.

3. The Collaborative plan for accelerating the review of medical devices and IVD

The Collaborative Plan for Accelerating the Review of Medical Devices was initiated after the Accelerated Review Action Program for medical devices. The Action Program and its excellent results are described in Chapter 2. Here, we introduce some of the major achievements of the medical device and IVD collaborative plan that was started in order to accelerate the review on the heels of the success of the Action Program.

3-1. Collaborative Plan for Accelerating the Review of Medical Devices

The Action Program described in Chapter 2 significantly contributed to eliminating device lag. To further accelerate the review process, both government and industry agreed to formulate a collaborative plan with a view to accelerate reviews by improving the quality of reviews and applications.

The target review period was set at the 80th percentile

value of the application cohort, which is higher than the 50th percentile value of the conventionally approved cohort. Setting the target values for both the reviewer and the applicant and debating who is responsible for delays is an unproductive discussion. Thus, instead of their individual holding time, the target value for the total review period was set.

In the discussion of how to name this initiative after the Action Program, it was impressive that we named it "collaboration"; hard work from both the government and industry to achieve their goals.

Collaborative Plan for Accelerating the Review of Medical Devices (FY 2014 - 2018)

Improve training of reviewers and quality of applicants
Review consultation system
Summarize ideas on clinical evaluations
Have a timeline in the standard process
Have a review checklist
Achieve a goal of total review period based on 80th percentile value of application cohort

3-2. Results of the Collaborative Plan for Accelerating the Review of Medical Devices

The collaborative plan was successfully completed at the end of March 2018. Activities and results for five years will be summarized. **Figure 2** shows the achievement of the target review period, which was one of the most fruitful results.

The AMDD, the Japan Federation of Medical Devices Association (JFMDA), and the EBC jointly carry out Time Clock Surveys every year. **Figure 2** compares the results of the survey at the start of the collaborative plan and the final fiscal year. The review period was shortened in all application categories, and the target value was achieved in almost all categories in the final fiscal year.

The biggest goal for both the Action Program and the Collaborative Plan was acceleration of the review. A new Collaborative Plan, started in April 2019, set "optimization of regulations and review" as a goal. While maintaining the current review period target, we seek to optimize the medical device development process and regulations.

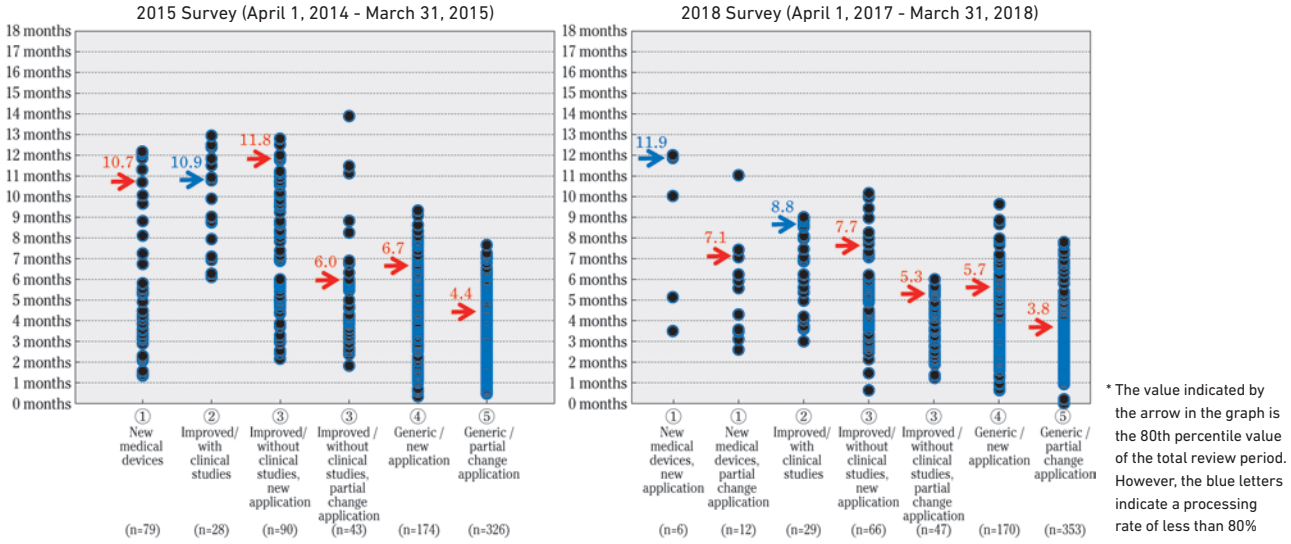
3-3. Collaborative Plan for Accelerating the Review of IVD

IVD had been still out of scope when the review acceleration action program was to be started in the medical device field. As a result of discussions between the then ACCJ Medical Device and IVD Subcommittee's RAQA Committee Chairperson (Junko Kodama) and the IVD Chairperson (Isao Ikeda), the IVD-TF was newly established under the RAQA Committee, and the regulatory system task force IVD-TF was then newly set up following the advocacy activities to the MHLW. It was in 2007 when participants from the ACCJ and JACRI came to the negotiating table at IVD-TF as representatives of industry groups, to set the stage for constructive discussions concerning IVD.

Until then, the IVD industry had mainly functioned as a bridge to conduct industry research and gather opinions upon request from the government. At the regular opinion exchange meetings on regulatory affairs between the medical device association and the government, time was allocated for the IVD industry, allowing the industry to voice their demands in public. However, people in the IVD industry group were not skilled at communicating their requests and discussing issues with the MHLW / PMDA; they were seen as a rather "sheepish industry group" (according to the MHLW). Looking at the preceding medical device industry as their role model, the IVD industry group became capable of creating materials that logically explained their views and having heated discussions within the industry.

In the Collaborative Plan for Accelerating the Review of IVD (2014-2018), dated March 31, 2014, the collaborative plan proceeded on the following matters:

• Improve quality in the approval review process



* The value indicated by the arrow in the graph is the 80th percentile value of the total review period. However, the blue letters indicate a processing rate of less than 80%

Figure 2. Results of Time Clock Survey (AMDD, JFMDA, EBC joint survey), application cohort 80th percentile value

Words from the Chairman

Former Chairman on 10 Years of the AMDD

Takashi Shimada, Third Chairman (2012 - 2015)

There were three major issues that I worked on during my tenure as the AMDD Chairman (2012 - 2015). Device lag, foreign average pricing (FAP), and revisions of the Pharmaceutical Affairs Law.

Based on the recommendations from the 2008 Device Lag Survey presented by the ACCJ, device lag improved dramatically through the 2009 MHLW Action Program for accelerating reviews at the PMDA. The issue of slow reviews had been discussed at the AMDD since the times of Chairman Wang and Chairman Powell. The data from the Time Clock Survey conducted by the ECB and the JFMDA, particularly helped them to objectively grasp the issue and to take actions for the resolution of issues.

The AMDD continues to call for the abolition of FAP, but it still remains a challenge. As a result of the implementation of FAP, Japan's reimbursement prices have gone down so low that Japan has become the least favored investment market. This "Japan passing" has created a device gap rather than a device lag, which calls for our attention.

Lastly, with regard to the revision of the Pharmaceutical Affairs Law, the Law had been regulating medical devices using the same legal framework as with pharmaceuticals. Medical devices are completely different from pharmaceuticals. For example, a drug has a compound which is something that is discovered. Approved compounds must remain unchanged. Whereas a medical device is something that is designed, used for treatment, and are to be improved over a short cycle. Subjecting medical devices to the same restrictions and regulations as pharmaceuticals was not logical in many way, and hampered innovation. We at the AMDD had had discussion after discussion with the MHLW almost every month, and were eventually successful in making them understand the differences between pharmaceuticals and medical devices. In November 2013, we were finally able to see the current Pharmaceuticals and Medical Devices Act (PMD Act).

I give credit for this success to enthusiastic cooperation of the committees set up within the AMDD. This is the strength and characteristic of the AMDD, which also impressed the staff at the US embassy.

Aside from those external issues, I also worked hard on internal group management. During my tenure, we saw M&A between member companies (J&J with Synthes, Medtronic with Covidien, Zimmer with Biomet, etc.), which raised the risk of decreasing membership fees. As this may have significantly impacted finances of the AMDD, which relies on membership fees, the membership fee system was overhauled during my tenure. We visited member companies and asked the top management to increase their contributions. That's one of the memories I recall. In addition, for compliance purposes, we made a rule that the AMDD comprehensively undertakes Foreign Corrupt Practices Act (FCPA) training with wholesalers. Our members and agencies welcomed this move.

I was extremely busy as I was representing my company both externally and internally while serving as Chairman of the AMDD. However, I was grateful for my position back then as it gave me the opportunity to think about patients deeply, not just from the perspective of a company but from that of healthcare public policy.

I hope the AMDD continues to make policy recommendations and work hard for the benefit of medical care and patients in Japan.

(AMDD adviser, former President of Medtronic Japan Co., Ltd.)

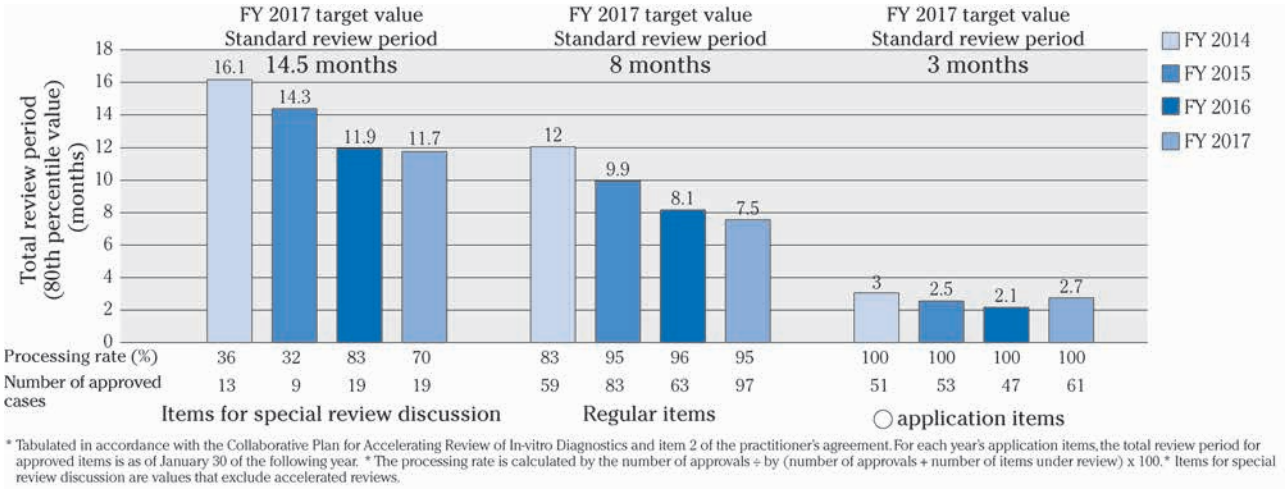
- Set a standard review period
- Increase reviewers
- Manage progress

The collaborative plan for accelerating review was a five-year plan, but a period for reviewing issues and goals was set during that time. As a result of the review, almost all unresolved issues; the regulatory system task force, proposals and discussions on law revision requests, are included in the collaborative plan. It is currently used as a history management tool for resolving issues of regulatory affairs. Examples of issues included during that period are as follows:

- Discussions on streamlining operations and approaches of pre-approval testing by the National Institute of Infectious Diseases (NIID).
- Global harmonization of review requirements and standards
- Reliability assurance of application dossiers
- Clinical performance testing guidelines
- Review of classifications

3-4. Results of Collaborative Plan for Accelerating Review of IVD

The final results of FY 2014 - 2018 collaborative plan will be released after the completion of analysis in 2019 - 2020. Preliminary figures compiled by the PMDA as of July 2019 are as shown in **Figure 3**. The review periods for the two categories (items for special review discussion, regular items) with set goals, were shortened year by year, and goals set for each year were met. With the understanding and cooperation of both applicants and reviewers, the data for the final year, FY 2018 application cohort, is also expected to meet its goal.



* Tabulated in accordance with the Collaborative Plan for Accelerating Review of In-vitro Diagnostics and item 2 of the practitioner's agreement. For each year's application items, the total review period for approved items is as of January 30 of the following year. * The processing rate is calculated by the number of approvals ÷ by (number of approvals + number of items under review) x 100. * Items for special review discussion are values that exclude accelerated reviews.

Figure 3. Total review period for in-vitro diagnostics (application cohort) (Source: Meeting of Collaborative Plan Practitioners, March 20, 2019)

4. Expectations for future revisions to the Pharmaceuticals and Medical Devices Act

As of July 2019, a bill on revisions to the Pharmaceuticals and Medical Devices Act has been submitted to the National Diet, pending deliberation. In April 2018, an industry group including the AMDD, JFMDA and EBC jointly submitted a proposal for revisions.

- Provide all provisions related to medical devices in a separate chapter.
- Further streamline QMS compliance inspection and international harmonization
- Promote the use of package inserts on electronic media

Additionally, after discussions with the government, matters related to the review system and traceability were also included.

- Early introduction of the approval review system tailored to the characteristics of medical devices
- Improve traceability of medical devices

The IVD industry also submitted proposals / revision requests from a joint team of the three IVD organizations (AMDD, JACRI, and EBC). "Request from the IVD Industry for a Revision of the Pharmaceuticals and Medical Devices Act," July 5, 2018

- Review of the definition of IVDs
- Review of licensing requirement for business category (marketing authorization, manufacturing, sales), and eligibility requirements of administrators, etc.
- Requests to streamline QMS compliance inspection
- Promote the use of package inserts for electronic media

As outlined above, in the previous revision of the Act, we enacted provisions for medical devices that are different from pharmaceuticals, with regard to marketing authorization and manufacturing of medical devices. In this recommendation for revision submitted by the medical device / IVD industry, a completely separate chapter for medical device provisions was requested as part of efforts to formulate a medical device act in the future. The recommendation included the establishment of a review system that can deal with new technologies such as AI. The AMDD would like to contribute by actively involving itself in the discussion and eventually realizing its requests.

5. Closing remarks

During the 10 years since the AMDD's inception, there have been significant changes in the relationships between the industry and the MHLW/PMDA.

At the time of inception, it was normal that approval was delayed by a year in comparison with Europe and the US because of regulations unique to Japan. And the AMDD, making efforts to improve the situation, was often accused of acting like an outsider pressuring Japan. However, we believe that our relationship changed to that of a collaborative stakeholder.

As our Association is increasingly globalized, real world and technological progress including big data and AI, continue to become more complex, and challenges will be more difficult to resolve. When we arrive at a juncture, we hope that our efforts over the past decade and the results we accumulated, together with the activities of our next 10 years can greatly contribute to tackling such challenges.

Reference

1) RAQA Committee Leadership Team, AMDD, "Medical Device Regulation Issues in Japan and their Solution", Pharmaceutical Medical Device Regulatory Science. Vol. 42 No. 11-12 (2011), Vol. 43 No. 1 (2012)

Contribution

What I have Witnessed in 10 Years of the AMDD

Yasushi Takahashi, Acting Chairman, Japan Association of Cardiac Pacemaker Friends (JACPF)

Congratulations to the American Medical Devices and Diagnostics Manufacturers' Association on your 10th anniversary. Allow me to express my heartfelt respect to the AMDD. As a medical device industry association within a diversified society, the AMDD has made a major contribution to the development of the medical industry and comprehensive management over the past decade through the dissemination and sharing of information to related parties.

JACPF's history begins in 1963 when the first domestic cardiac pacemaker (hereinafter, "PM") was implanted at the University of Tokyo Hospital. The establishment of our association was prompted by necessity to share patient information. The activities of JACPF got under way through the efforts of Dr. Kansai Hayakawa, our first president and the first doctor to have a PM implanted. In 1993, he received the Health Culture Award for his contribution and was admitted to be in the presence of the Emperor.

We PM wearers benefit greatly from the development of medical devices and we pin our hopes on their further progress.

Association members have PMs/ICDs under their collarbones and in their abdomens, and these devices send electrical signals for symptoms associated with bradyarrhythmia.

The first implanted PM had a built-in mercury battery of 8 centimeters in diameter. It started out as an external system with a battery-life of only one to two years; it placed a heavy burden on the patients. PMs fall under the medical device class IV, "specially controlled medical devices, they may be linked to a life-threatening crisis in the event of malfunction".

However, thanks to the remarkable research and development in medical devices since then, significant progress has been made in PM compared with the one we first implanted 41 years previously. Downsizing of PM with batteries changing from mercury to lithium enabled MRI imaging and home monitoring with a transmission system. In 2016, the successful development of a leadless PM was announced, and battery life is now over 12 years. Such PMs are being implanted for those patients indicated for the devices.

Approximately 520,000 to 560,000 PM wearers are now in Japan. Of which, JACPF members account for 3,600 members across 29 chapters around the country. Above all, JACPF, as a patient group representing sufferers of the same disease, values mental care. Our fundamental principles are "appreciation, gratitude, and service." We are not a demanding organization. We shared information with the Japan Association of ICD Friends and the National Association for the Protection of Children with Heart Disease and promoted our activities.

We would like to thank you for your warm support. We would not be here today were it not for support from the AMDD, government, academic societies, universities, hospitals, and medical device companies.

Amid the recent progress in medical care and medical devices, PM patients now have a sense of security/QOL in their lives and are able to participate in society just as they did before the implantation of the devices.

That said, PM patients get older and their declining physical strength is inevitable although they look healthy. To address the anxiety of infections, when a PM or old batteries are replaced, we hope that one day implanted PM batteries can be charged from outside the body to prolong battery-life.

Medical development is a critical concern for patients. Many people suffer from various intractable conditions, sudden heart and brain diseases, and malignant tumors that develop one in every two persons. Such a status led us to consider the following points:

1) Increase the chances of early detection with preventive medicine.
   Correct diagnosis and early treatment initiation are vital to a patient's survival. I have been admitted to the hospital 10 times and experienced a series of painful tests and operations. Public health checkups offered by municipalities are often simple and may fall short from early detection of problems. We hope that the burden on patients will be reduced by the development of medical devices that allow more tests and less pain for patients.
2) No healthcare disparities among medical institutions and by region.
   This is a university hospital-oriented issue, but the family doctor system must be improved. It is still difficult for patients to ask for a second opinion. Elderly patients express their discontent in the way doctors address their complaints as doctors tend to blame everything on aging.
3) Reforms are under way to review clinical issues and promote acceleration of approval process for treatment drugs. We would like to realize a system that provides patients with great healthcare.
   Meanwhile, patients should be proactive in their own treatment, not totally dependent on medical professionals. They should ask their doctors questions to deepen their understanding and to their circumstances as patients, and fight and live with their illnesses.

Healthcare is the most important aspect for human beings as it is related to the dignity of life. On a personal note, I would like to express my heartfelt respect to those who work day-in-day-out in research and development, as I would not have survived if PM had not been developed.

Finally, we would like to express our deep appreciation for the regular and valuable dissemination of information by the AMDD that performs an important role in the medical industry in developed countries, and we look forward to your continued guidance.

I end my note by wishing you the best for your future endeavors.

In-vitro Diagnostics (IVD)

IVD were first defined in 1985 under the Pharmaceutical Affairs Law. Since then, laws and regulations for IVD and insurance coverage rules for medical fees have been developed. Along with progress in testing technology and shifts in social and medical environments, the value and positioning of clinical testing have significantly changed. IVD are not only used for disease prevention, diagnosis, decision on treatment policy and clinical monitoring of prognosis, but also for various clinical settings for purposes other than diagnosis, such as companion diagnostics (CoDx) to stratify patients for drug administration.

Looking back over the past decade, as innovations in the IVD field that have made significant contributions to improving patient outcomes, we introduce CoDx and tests before medical examination.

The advent of CoDx

CoDx is a biomarker testing IVD used mainly for predicting the efficacy and safety of a drug and optimizing the dose of a drug in pharmacotherapy including anticancer drugs. It is expected to be widely used in future medical care, and to be indispensable for personalized medicine, enabling selection of treatments and medications suited to individual patients.

Pharmaceutical companies and diagnostics manufacturers develop a drug and CoDx concurrently, and market them almost simultaneously after PMDA review. This requires unprecedented innovative development process, review process, and insurance coverage based on a new idea. Thus, diagnostic manufacturers created a new process in collaboration with pharmaceutical companies, and the PMDA / MHLW. Since 2012 when the first CoDx was approved as an IVD, several CoDxs have been approved and covered by insurance.

The introduction of testing before medical examinations

Testing before medical examination is clinical testing performed prior to medical examination by doctors for outpatients. The patient sees the doctor after the test results are obtained. With the introduction of this testing, test results are available in a timely manner, and patients can receive appropriate treatment without revisiting the hospital to verify the test results or take additional tests. This resulted in changes in patient behavior and daily living since social activities are not restricted due to hospital visits.

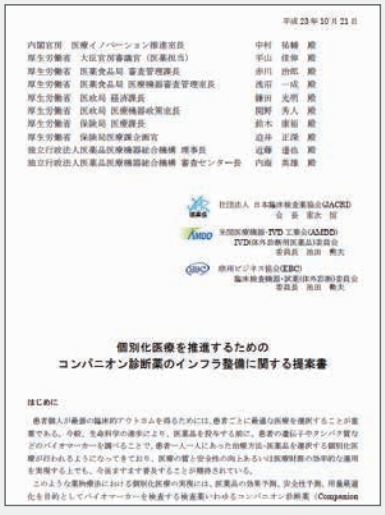
Testing before medical examinations was introduced in the clinical setting more than 10 years ago. Diagnostics manufacturers not only pursued the automation and shortening of testing time, but also requested Chuikyo to add points of outpatient rapid clinical testing within medical fees, in cooperation with academic societies related to clinical testing. In 2006, a new calculation was implemented. Initially, one point was added for each item, up to 5 items. However, test-related academic societies, manufacturers, and industry groups pressured the government, and the calculation was changed to the addition of 5 points for each item in 2008, and the addition of 10 points for each item in 2010. We were also successful in our policy guidance to implement tests before medical examinations for medical institutions.

The two examples above were achieved through a combination of innovation in the regulatory system related to clinical testing and innovation in testing technology. Above all, innovation of the regulatory system could not have been achieved without collaboration between industry groups such as the AMDD and stakeholders.

To contribute to a prolonged healthy life span, we continue with our activities to improve testing technology and design and optimization of the regulatory system including the introduction of a specimen measurement room (2014), and addition of an item for OTC IVD for the first time in 25 years (2016).

The role played by clinical testing will be more diversified and its continued contribution to the healthy lives of the public is expected as shown in: the Global Action Plan on Antimicrobial Resistance (AMR), which was adopted at the 2015 World Health Assembly and further mentioned at the 2018 G20 held in Argentina; the contribution from Japan's action plan; early detection of cancer with microRNA testing; and the promotion of testing information management using ICT. In December 2018, cancer-related multigene panel testing obtained the first regulatory approval in Japan as a combination medical device, and its insurance coverage began in June, 2019. Multigene panel testing has the potential to significantly change the future of medical care and people's lives. Thus, while hoping and anticipating its future development and prevalence, we will watch closely the insurance coverage of panel testing and the possibility of recalculation upon its market expansion.

A page, set up on the PMDA website for the companion diagnostics WG



Paper on a Joint Position of three IVD organizations: Proposal on Infrastructure Development for Companion Diagnostics to Promote Personalized Medical Care

Diabetes (A New Era of Glucose Monitoring)

In recent years, survey results showed that 10 million adults in Japan are strongly suspected of having an diabetes, an alarming statistic where diabetes is a national disease. Various drugs are used for treatment; however it is important to know a patient's glucose level in detail before selecting medication / determining effects or giving guidance on medical treatment. The Japan Diabetes Society (JDS) says that not only medical professionals but also patients themselves should understand in detail their own glucose fluctuations, especially those who are taking insulin.

Glucose monitoring technology development started with the advent of urinary sugar test strip in the early 1900s. Now, glucose levels can easily be measured with a simple self-monitoring blood glucose meter. Blood glucose must be measured frequently at appropriate timing to grasp glucose fluctuations in detail. However, self-measurement of blood glucose presented issues including pain due to fingertip pricks and the inability to obtain glucose levels other than measured points in time.

In 2009, a Continuous Glucose Monitoring (CGM) system that continuously measures the glucose concentration in interstitial fluid became available. The CGM captured in detail glucose fluctuations that had been difficult to grasp. Thereafter, the concept of "quality of glucose control" attracted more attention. Treatment to avoid hypoglycemia and minimize glucose fluctuations has been sought. The CGM back then was designed for professional use; medical professionals used it to obtain detailed data and it required specialized knowledge to analyze data. Its specifications did not allow patients to check data in real-time by themselves. Then, a system that allowed patients to check their glucose fluctuations in real-time was marketed, but such functions were accompanied by the insulin pump, and its use was limited to few patients.

In January 2017, a Flash Glucose Monitoring system* was launched in Japan. It was a system that allowed patients for the first time to check their glucose fluctuations in detail. Unlike other CGM systems, it did not require daily calibration, saving time for healthcare workers and patients alike. It has been clinically adopted as a monitoring system that allows both healthcare professionals and patients to quickly and easily grasp glucose fluctuations. In December 2018, clinical application of real-time CGM** started. This enabled real-time monitoring of glucose for non-insulin pump users. With real-time CGM, patients can check their glucose fluctuations, and be alerted for hypoglycemia or hyperglycemia, thereby allowing them to take early actions against hypoglycemia and hyperglycemia.

These systems make glucose fluctuations visible, enabling strategic treatment planning, medical guidance, and changes in patient behavior. This is expected to bring better glucose control. The waves of digital transformation are also affecting the field of diabetes; as we move into the future, with the expansion of the eco-system and further incorporation of AI, the distance between patients, healthcare professionals and caregivers will be considerably narrowed, and the level of diabetes treatment will be further enhanced.

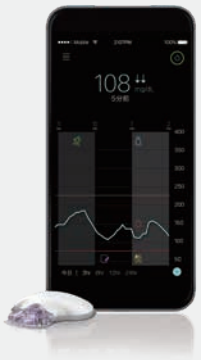
* Flash Glucose Monitoring system

A sensor the size of a 500-yen coin is attached to the back of the upper arm, and the data stored in the sensor is read by scanning it with the reader (main unit). Scanning the sensor, a patient can check and confirm their current glucose level, changes in their glucose level over the preceding 8 hours, and future glucose trends. The sensor can be easily attached, and it measures glucose levels continuously for up to 14 days without the need for calibration that requires the fingertip prick. (A device for medical professionals is also available. A patient wears only the sensor and has no reader, and the medical institution reads the data.)

Flash Glucose Monitoring system

** Real-time CGM

In real-time CGM, a sensor electrode that is as fine as a hair is placed under the skin and connected to a transmitter for continuous measurement of subcutaneous glucose, and the data is then continuously sent to a monitor. Patients can monitor their own glucose fluctuations in real-time, and can receive alerts should hypoglycemia occur. In 2015, an insulin pump that can display real-time CGM on screen became available in Japan, and in 2018, a pump that automatically suspends and resumes insulin administration based on those CGM values was also rolled out. At the end of 2018, a device was launched, which allowed even patients receiving insulin pen injections to check real-time CGM on a mobile device or on a dedicated monitor, and share data with family members and medical professionals.



Real-time CGM

Chapter
4

Changes in the Insurance Reimbursement System for Medical Devices and In-vitro Diagnostics (IVD) over 10 Years and AMDD's Response

The following describes the changes in the special treatment material system since the AMDD was founded in 2009, and how the AMDD has addressed those changes, and touched on future issues.

1. Changes in the insured special treatment material system and AMDD's response

The insured special treatment material system was created based on the recommendations of the Central Social Insurance Medical Council (Chuikyo) in 1993, and by 2002, the framework of the current system was in place. Subsequently, the system was reformed in line with revisions of medical fees.

The Chuikyo Committee on Medical Materials is an advisory body for medical fees, a place for practical decision-making, and the main battlefield of the medical devices reimbursement system. The items targeted were fundamentally special treatment materials, and the focal areas were the evaluation of innovation and the correction of domestic and foreign price gaps. However, in recent years, technical fee inclusive systems including large-scale medical devices and IVD are also covered by the expert group. In this article, these elements are described sequentially.

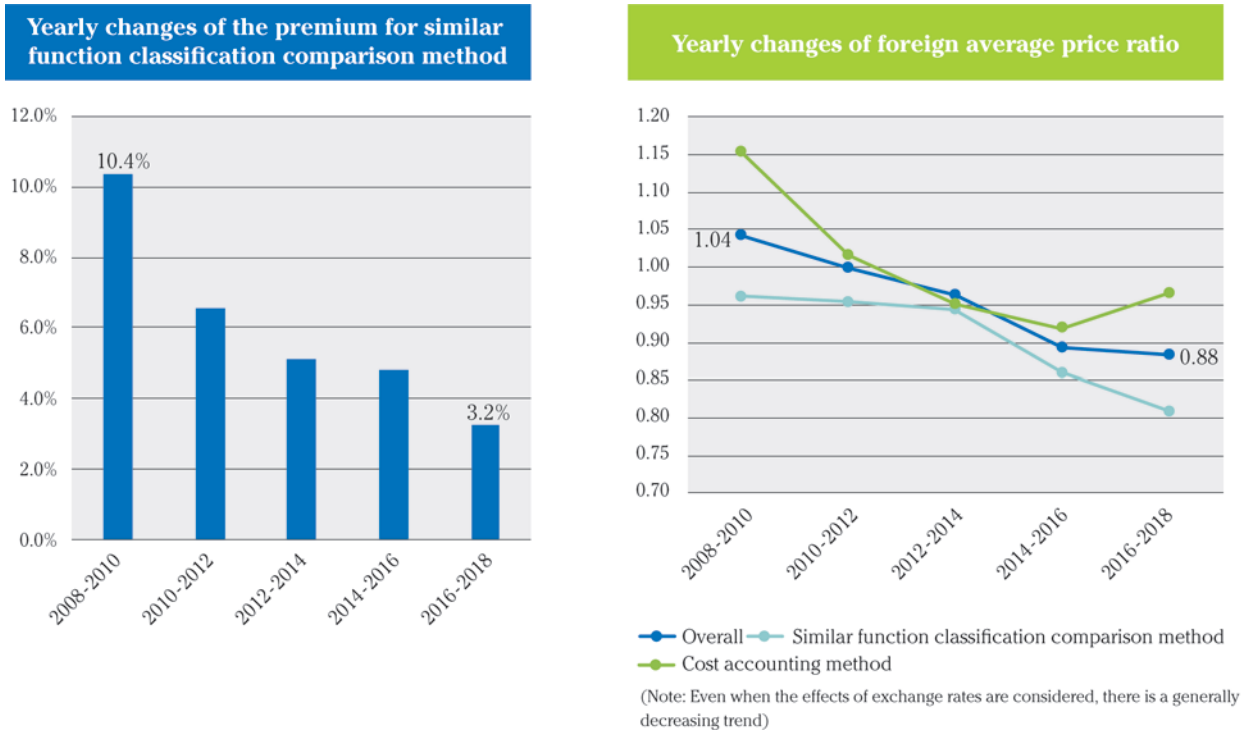


Figure 1. The premium rate and the foreign average price ratio have been decreasing over the past 10 years

1) Evaluation of innovation

The reimbursement price for Japanese medical devices (specially insured medical materials) is reduced by the market price and the foreign average price once every two years when it is revised [1]. For medical devices that are not listed by brand but are listed by a function classification that share similar structure and indications, the price is reduced not only by the company's market price or foreign average price but also by the market price of competitors' products. It is extremely important that appropriate evaluation of innovation is made when new products are introduced in order to secure funds for future R&D.

Enhancements and improvements of the premium method

Methods for evaluating new products are 1) the similar function classification comparison method and 2) the cost accounting method. The similar function classification comparison method includes a premium for innovativeness, usefulness, and marketability, and a premium for improvement which has been included since 2008.

Since 2009, the Government's policy to promote the medical device industry has also introduced the following matters sequentially for innovation evaluation:

1) Evaluation for expedited insurance coverage
2) Review of premium for improvements (evaluation of high probability, additional requirements, etc.)
3) Special cases of function classification

The AMDD's awareness of issues and response

Although these systems have played a certain role in promoting innovation, AMDD has been aware since 2015 that conventional evaluation of innovation is insufficient to secure the spiraling costs of R&D.

Looking at the average premium rate of the similar function classification comparison method, the decrease to 10.4% in 2008 - 2010, 6.5% in 2010 - 2012, and 5.1% in 2012 - 2014 can be seen. When compared in foreign prices, prices in Japan are lower. (See **Figure 1**.)

As a result of heated discussions within the AMDD, value-based healthcare was proposed in 2017 (see **Figure 2**.) with the support of external organizations.

Specifically, the AMDD proposed to introduce economic evaluation as the fourth supplementary premium requirement, and the establishment of a novelty leading evaluation system. The idea was to make both "promotion of innovation and ensuring medical access for patients", and "sound medical and nursing care finance" possible.

The AMDD had made various recommendations on system reform up to that point, but it had never made a comprehensive proposal with a view on financial soundness. This proposal was well received by various stakeholders.

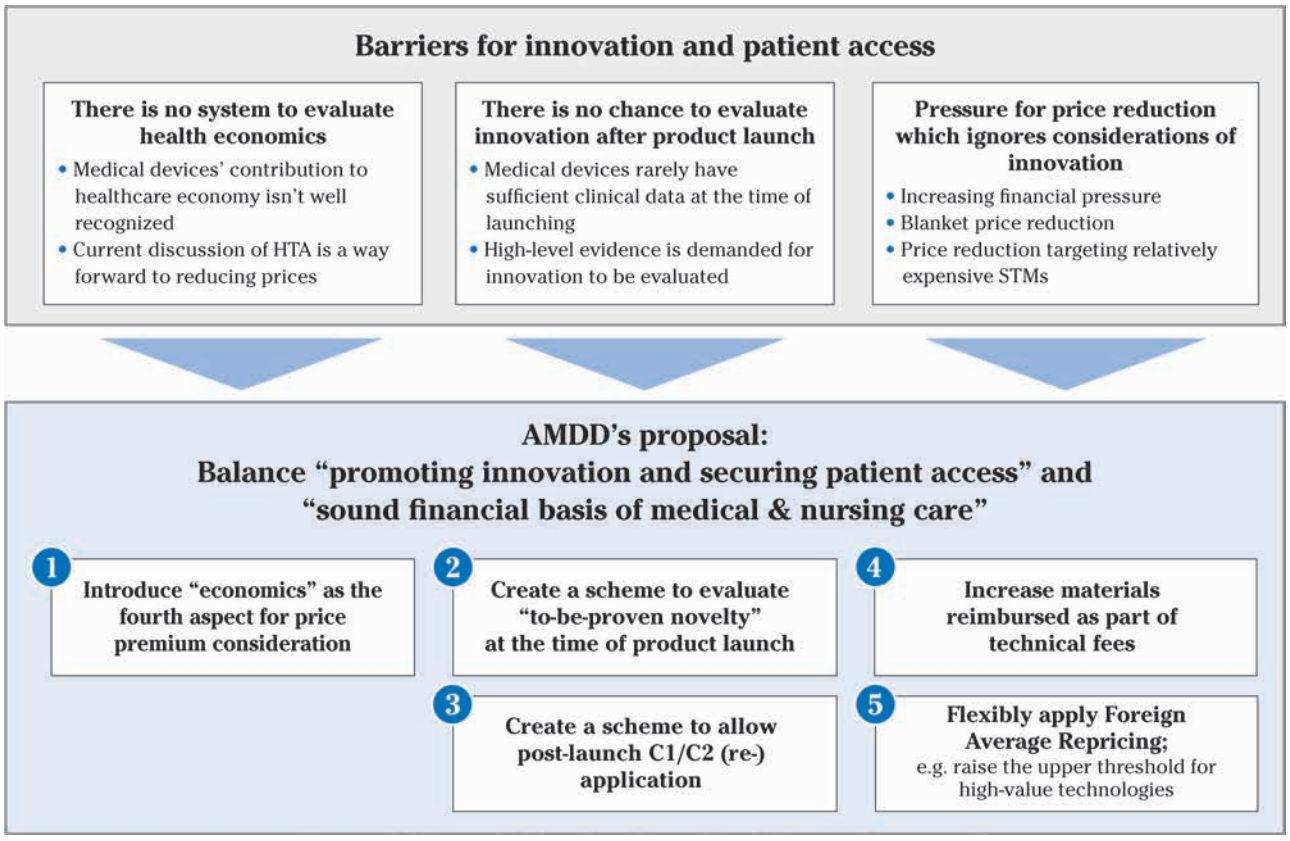


Figure 2. Value-based healthcare

Subsequent introduction of the new system

This led to the "challenge application" which was introduced in 2018, and the "price hike" rule in the cost-effectiveness evaluation system, which was introduced in 2019.

The "Challenge application" is a system for long-term implantable devices, which allows applicants to apply for a new function classification after it is covered by insurance based on clinical use records if sufficient clinical data cannot be ready for the insurance coverage. "Price hike" in the cost-effectiveness evaluation system means to raise the reimbursement price if the result of analyzing the cost-effectiveness evaluation shows that the incremental cost-effectiveness ratio (ICER) is less than 2 million yen, or if effectiveness is equal or higher and cost goes down. Both cases are in line with AMDD's recommendations.

As these two cases are not sufficient for the evaluation of innovation, the AMDD should continue to make recommendations in line with value-based healthcare, and make these new systems more desirable.

2) Domestic and foreign price gap

It was pointed out in the 1990s that medical devices in Japan seemed to be priced higher than overseas. In order to correct this gap, a system for lowering prices, FAP, when Japanese prices are higher than the FAP by a certain ratio (the upper limit of the foreign price rate) was introduced in 2002 (foreign price adjustment for new products and recalculation system for existing listed products). Since then, even stricter rules for remedying differences between domestic and foreign prices have been in place, such as lowering the upper limit of the foreign price rate and introducing outlier rules.

AMDD's awareness of issues and response

With AdvaMed, the AMDD has consistently presented a variety of evidence to Chuikyo to oppose the uniform price cut that does not factor in differing market environments which result in differing prices from country to country.

In 2009, the AMDD entrusted the research to Mitsubishi Research Institute. Results showed that cardiovascular medical devices cost 2.2 times higher in Japan than in European countries, and orthopedic devices cost 2.5 times higher [2].

In 2011, the AMDD announced "Comparison Survey of Market Environment for Medical Devices in Japan, China, and Korea". The results indicated that a device lag and device gap between Japan and China/Korea had emerged, not to mention such gaps between Japan and Europe / US. We argued that the abolition of the FAP adjustment system was necessary to resolve this gap [3].

In 2015, the AMDD revealed in cooperation with the Japan Medical Device Sales Association and organizations in Japan and Europe that the implementation bodies for product distribution and proper usage support for the supply and distribution of medical devices are different in Japan and Europe; and that the differences in the number of medical institutions in Japan and Europe, the intensity of cases and the structure of medical institutions, were addressed by manufacturers and distributors [4].

The evidence which the AMDD submitted was positively received by Chuikyo bodies and government officials as it is useful to understand the actual state of the medical device market and the provision system. There used to be an emotional repulsion to the foreign and domestic price gaps, but the current environment allows evidence-based discussion.

The volatile fluctuation of foreign exchange from the second half of 2000 to the first half of 2010 triggered concerns over a major impact on reimbursement prices. Then, the MHLW and Chuikyo showed a certain level of understanding of how to mitigate radical changes from the impact, and came up with a specific measure to extend the target period for calculating exchange rates.

On the other hand, the prices of medical devices in Japan sequentially fell due to not only the FAP system but also the so-called R-zone system, in which prices are cut in accordance with the market prices. Some product prices have fallen by 10 - 15% at every revision. As outlined earlier, the price of new products in Japan is lower than overseas prices on average, and Chuikyo has pointed out that the price gap between domestic and foreign countries has shrunk considerably.

3) Technical fee inclusive products

The treatment material system and the expert committee on special treatment materials at Chuikyo have been positioned as a forum for the discussion of special treatment material.

Meanwhile, the medical device industry and IVD industry groups, including the AMDD, have requested that the evaluation process and the methods used for evaluations of new products, such as diagnostic imaging and IVD (including those other than special treatment material) should be clearly defined, and the groups requested opportunities to state their opinions at Chuikyo [5].

Against this backdrop, it was gradually becoming clear that: C2 applications for technical fee inclusive products would be possible; companies can request the applied technical fees from 2016; organizations dedicated to treatment material can propose the applied technical fees to Chuikyo; IVD can be included in the discussion of new product evaluation at dedicated treatment material organizations; and opinions can be stated at the expert committee on special treatment materials at Chuikyo.

While technical fee inclusive products are increasing,

underpinned by the medical device program established by the Pharmaceuticals and Medical Device Act (PMD Act) of 2014, there is a need for further clarification of the insurance reimbursement process related to technical fee inclusive products.

2. The establishment of the Medical Technology Policy Institute (MTPI)

In October 2017, the AMDD established the MTPI. In a press release, Kosuke Kato, Chairman of the AMDD, said, "The AMDD's earnest wish is to see the high-quality, advanced medical technologies of AMDD member companies make Japanese healthier. However, with tight financial positions in Japan, it is not easy to introduce the latest technologies in a timely manner to please everyone. Under such difficult circumstances, the AMDD established MTPI to carry out research from a mid- to long-term perspective on how medical devices and IVD can contribute to Japanese medical care and to make policy proposals based on the research."

The AMDD had experienced that evidence-based policy proposals and comprehensive proposals in consideration of sound financial positioning (value-based healthcare) had been well received by related parties, and considered it necessary to accumulate more discussions from a public perspective over the medium- to long-term. This led to the establishment of MTPI.

Since its establishment, MTPI has been providing information through research papers [6)-9)] and supporting research groups with academia [10)] in relation to the Japan Association for the Advancement of Medical Equipment (JAAME) and various AMDD committees.

In May 2019, as part of an effort to promote collaboration with external experts and to enhance functionality, the AMDD invited Kohei Onozaki, director of the Japan Health and Global Policy Institute, on board as a special advisor, and Kosuke Iwasaki, Actuary and Milliman Tokyo Office Director, on board as a senior researcher.

3. Challenges that lie ahead of us

Japan has an unprecedented declining birthrate and aging population. According to "the Social Security Toward 2040" depicted by the MHLW, it is important for us to somehow manage the current situation until 2040 when the number of elderly people levels off or slightly decreases. To that end, the two major policy issues are to curtail increases in medical expenses by prolonging healthy life spans, and to maintain social vitality and secure medical and nursing care services through improved productivity amid a rapidly shrinking workforce.

When the AMDD considers the relationship between these policy issues and medical devices, it can be expected that the extension of a healthy life span will be seen if more and more advanced medical devices, including those related to heart failure and orthopedics which contribute to improved QOL of elderly, are developed and introduced.

Improved productivity is expected to reduce physical and psychological burdens of healthcare professionals through technologies including robots, IoT, monitoring, and AI.

Medical devices are expected to make a major contribution to Japan's two major policy issues. To allow medical devices an even greater role to play, the AMDD must anticipate changes in Japan's medical policies and markets, and address those changes.

There are currently three changes in the future of healthcare policy / market access.

Value-based healthcare

First change is the trend toward value-based healthcare that was proposed by the AMDD. Value-based healthcare includes the introduction of cost-effectiveness assessment, which is not only based on medical technology sophistication, but also on the reimbursement of medical expenses according to the results achieved, instead of the treatment given (shifting from a quantitative basis to a qualitative basis); and the reimbursement based on medical expenses required for a series of treatments per patient in addition to the medical expenses required at individual medical institutions (bundle payment).

Even if a medical device that can reduce the burden on healthcare professionals is introduced, if the medical expenses are paid based on performance, the income of the medical institution will not decrease. If bundle payments prevail as a payment method, even if the initial medical expenses are relatively high, products that can reduce medical expenses for readmission will be more valued in the clinical setting.

Digital health / IoT

Second change is a trend of digital health / IoT. Digitization related to our daily lives is now inevitable, and of course, the digitization of medical technology will also progress. It has been more than 10 years since the introduction of technology that enabled the remote monitoring of pacemakers. In that sense, it can be said that digital health started a long time ago in the medical device industry.

With the revision of medical fees in 2018, the remote monitoring premium of the pacemaker guidance management fee is now nearly three times what it was in the past, and the evaluation of remote monitoring for other technologies including CPAP has also evolved. If such evaluations continue and digital health and IoT are further implemented, longer healthy life spans and improved productivity can be expected to be seen.

Expansion of the shared billing scheme

Third change is the expansion of the shared billing scheme. A research group at the Institute for Health Economics and Policy (IHEP) in Japan published the report, "Review of the scope of coverage for public medical insurance," in June 2019. Within the report, IHEP recommended the expansion of the shared billing scheme, which may expand the use of medical devices.

For example, the report states that if the scope of applicable medical insurance is narrower than the scope approved by the PMD Act, then it should be clearly positioned under the shared billing scheme. Self-monitoring blood glucose meters and implantable cardioverter defibrillators are mentioned as examples of such cases. Such new coverage may expand options for more use of medical devices in medical settings.

4. Afterword

When the AMDD looks back at the past decade of the reimbursement system for medical devices and IVD in Japan, the AMDD has played a leading role in cooperation with Japanese and European organizations. Going forward, the AMDD looks forward to lead the industry together with the administrative authorities to contribute to the social security and healthcare system in Japan amid declining birthrates and an aging population.

Reference

1) There are exceptional cases where prices were raised, such as when products are unprofitable, or in the case of "challenge application" introduced in 2018.
2) AMDD: "Comparison of Medical Device Supply Costs in Japan and Europe", July 2009, https://amdd.jp/pdf/activities/recommen/report090724.pdf
3) AMDD: "Comparison Survey of Market Environment for Medical Devices in Japan, China, and Korea" , August 2011, https://amdd.jp/pdf/activities/recommen/report110921.pdf
4) Chuikyo Opinion Statement: "Survey on Differences in Supply and Distribution of Medical Devices in Japan and Europe", September 9, 2015, https://www.mhlw.go.jp/file/05-Shingikai-12404000-Hokenkyoku-Iryouka/0000096891.pdf
5) Request for IVD (from AMDD) - Chuikyo Insured Special Treatment Materials Expert Committee Statement , November 11, 2015, https://www.mhlw.go.jp/file/05-Shingikai-12404000-Hokenkyoku-Iryouka/0000103783.pdf
6) "What is meant by value-based healthcare (value-based healthcare)" Social insurance periodic report, 2700: 34-40, 2018
7) Reimbursement pricing for new medical devices in Japan: Is the evaluation of innovation appropriate? International Journal of Health Planning and Management, 2018 Dec 14. https: //doi.org/10.1002/hpm.2719
8) "Analysis of the relationship between the number of CT devices and MRI devices installed, the number of images taken, and medical costs, https://amdd.jp/about/mtpi.html
9) "Evidence of Digital Health", Beyond Health (Nikkei BP)
10) JAAME: "Announcement of the launch of the Medical Devices and Socioeconomic Research Group", http://www.jaame.or.jp/mdsi/other-files/mdse_press_release_20171031.pdf

History of main pricing rules set in the system of special treatment materials

Period	Main measures
October 1958	• Notification of film redemption prices (classified by function) • Reimbursement of municipal purchase price of splints as a special treatment material
November 1967	• Dialyzer (then named "cellophane for dialysis") insurance coverage (purchase price reimbursement)
March 1968	• Pacemaker insurance coverage (purchase price reimbursement)
February 1978	• Dialyzer was included in artificial kidney procedure fees
June 1981	• Dialyzer was separated from artificial kidney procedure fees • Notice of dialyzer reimbursement prices (classified by function)
April 1990	• Some special treatment materials including automatic suturing devices were included in procedure fee
April 1992	• Notice of brand-based reimbursement prices of pacemaker • Intraocular lens insurance application (evaluated by including procedural fees from start)
September 1993	• Chuikyo proposals (hereinafter "pricing based on proposal") Problems pointed out for treatment materials reimbursed at the purchase price: medical institutions are less likely to be cost conscious; competition principle is less likely to work in market price formation; and the same treatment materials have different redemption prices depending on medical institutions.
April 1994	• Notice of reimbursement prices for 7 items* such as artificial joints (classified by function) *Artificial joints (knee joints, hip joints), artificial heart valves (mechanical valves, bio-valves), disposable artificial heart-lung, balloon catheters for balloon pumping, percutaneous coronary angioplasty catheters
April 1996	• Notice of reimbursement prices for 16 items* such as angiography guide-wire (classified by function) *Guide-wire for angiography, sheath introducer set / dilators for angiography, catheter for angiography, catheter guide-wire for percutaneous coronary angioplasty, disposable catheter for bladder indwelling, optional components for artificial hip and knee joints, inner splints for fixing, esophageal varices sclerotherapy set, endoscopic esophageal varices ligation sets, cannulas extracorporeal circulation, guiding catheters for percutaneous coronary angioplasty catheters • Review of dialyzer grouping • Special sutures and back support belts are included in procedure fees
April 1998	• Review of a certain range in the revision of reference treatment material price • Addition of facility standards for pacemakers, PTCA, etc.
April 2000	• Special provisions limited to FY 2000 in association with the reduction of a certain range (range adjustment) • Measures for international price fluctuations of precious metal material for dental use (range correction)
October 2000	• Review of function classifications for pacemakers, PTCA catheters, and artificial joints • Abolition of municipal purchase price system (actual purchase price system) • Outline of procedures for determining new product classifications (including provisional price of C1) • Outline of procedures for setting new function classifications upon material price revisions • Establishment of an organization dedicated to treatment materials
April 2002	• Formulated the calculation method for the reimbursement price of special treatment materials for new function classifications (C1 and C2) when reviewing the definition of existing functional classifications and when setting up new function classifications. • When a new function classifications is set up, in principle the similar function classification comparison method is used. If there is no similar function classification, then use the cost calculation method. • If the calculated price is significantly different from actual market prices of other countries, certain price adjustments will be implemented • Recalculate fields that meet certain requirements with an aim to optimize the price of existing treatment materials • Review existing function classifications when material prices are revised
April 2004	• Review price adjustment criteria in the calculation of material prices for special treatment materials that require the setting of new function classifications (C1 and C2) • Insurance coverage for special treatment materials classified as C1 four times a year (Note) C2 (new function / new technology) insurance coverage, timed for the introduction of new medical technology insurance coverage • Review recalculation price adjustment rules • Review a certain range of reference material price revision
April 2006	• Insurance applied four times a year for classification C2 (new function / new technology) • Specified range review of reference material price revisions • Expanded scope of special treatment materials for which validity of recalculation conditions are discussed • Review measure to mitigate radical changes during recalculation
April 2008	• Review supplementary premium • Review new medical materials and recalculation price adjustment rules • Review a certain range of reference material price revisions • Raise objections
April 2010	• Review new medical materials and recalculation price adjustment rules • Handling of product cost within the cost accounting method • Review of statement on improved premium requirements • Review of a certain range of reference material price revisions • Clarification of rules for withdrawal of insurance coverage • Clarification of procedures for materials that are not fully reimbursed due to extremely difficult supply • Review of as-needed revision rules of the prices of precious metal for dental use
April 2012	• Review of new medical materials and recalculation price adjustment rules • Australia was added to foreign price reference system • Handling of post-marketing surveillance (PMS) costs within the cost accounting method • Review of supplementary premium requirements (clarification of target materials of premium, etc.) • Establishment of evaluations for expedited insurance coverage • Response to volatile foreign exchange rates
April 2014	• Review of price adjustments related to new function classifications (FAP calculation method, measures for products with very a low FAP ratio) • Review of the evaluation of innovation related to new function classifications (continue evaluation for expedited introduction of insurance, operating profit ratio in cost accounting method, special exceptions for function classifications, added additional requirements for supplementary premium) • Matters related to recalculation of existing function classifications (review of recalculation ratio, response to changes in consumption tax rate) • Review of reference material prices • Review of function classification • Measures for ensuring stable supply
April 2016	• Review of price adjustments in new function classifications (review of comparison levels, refinement of measures for products with a very low FAP ratio) • Review of evaluation of innovation in new function categories (evaluation of medical devices with high medical needs, continued evaluation and review requirements of expedited insurance introduction, continuation of special exceptions for function classifications, addition of approach to re-calculation by similar function classification comparison method, clarification of approach to C2 classification) • Review of recalculation of existing function classifications (revision of comparison levels, review of FAP calculation method) • Accelerated insurance coverage
April 2018	• Review of price adjustments related to new function classifications (FAP calculation method) • Measures for products that require evaluation based on actual usage, (operation of premium for replacement products, measures for new products that have been more simplified than existing products, continued evaluation and review of requirements for expedited introduction of insurance, continuation and expansion of special exceptions for function classifications) • Review of recalculation of existing function classifications (review of FAP calculation method) • Price adjustments premised on evaluation results in trial introduction of cost-effectiveness evaluations • Establishment of new insurance coverage classifications and simplified procedures
April 2019	• Introduction of cost-effectiveness evaluation (inclusion criteria for items covered, analysis process, price adjustments)

Source: FY 2016 "Guidebook on Insurance Coverage of Medical Device", a project commissioned by Economic Affairs Division, Health Policy Bureau, MHLW (March 2017, Mitsubishi UFJ Research & Consulting)
Data in the guidebook was simplified as needed and the change in the system from 2018 onward was added. Notation of years changed to the Gregorian calendar (CE).

Dialysis

Kidney disease

The kidneys are a pair of bean-shaped organs, located in the upper abdominal area of the human body. The kidney is an essential organ for maintaining the health of the body. Its main functions are to: 1) remove waste from the body, 2) maintain overall fluid and salt balance, 3) control blood pressure, 4) adjust the amount of red blood cells, and 5) maintain healthy bones.

In this way, the kidneys play an important role in human life. However, should the function of the kidneys gradually decrease due to aging, diabetes, high blood pressure, and arteriosclerosis, a patient may be diagnosed with chronic kidney disease (CKD), and require treatment depending on the condition of disease progression. Currently, approximately 13.3 million patients suffer from CKD, which is said to be a new national disease.

Treatment of CKD involves the combination of numerous methods, including lifestyle improvements, diet, treatment for high blood pressure, and pharmacotherapy. In serious cases, kidney function drops to 15% or less and renal replacement therapy including dialysis or renal transplant must be initiated.

Dialysis treatment

One renal replacement therapy is hemodialysis. This therapy circulates blood outside the body through an artificial filter to remove waste and excess water accumulated in the blood due to renal failure.

The prototype of the dialysis membrane used in treatment was invented by Thomas Graham in the mid-19th century. Doctor John Abel first applied the membrane as a substitute for the kidney in 1913, and successfully performed extracorporeal hemodialysis on animals. Initially, blood coagulation during extracorporeal circulation was a major challenge. However, anticoagulants have been developed subsequently, and the procedure could be performed on the human body.

Since the end of World War II, dialysis technology dramatically improved. Downsizing of devices prompted the enlargement of the dialysis membrane area. During the process, multilayer dialyzers and hollow fiber dialyzers were developed. After a number of improvements, this became the standard therapy up to now.

Principles of hemodialysis

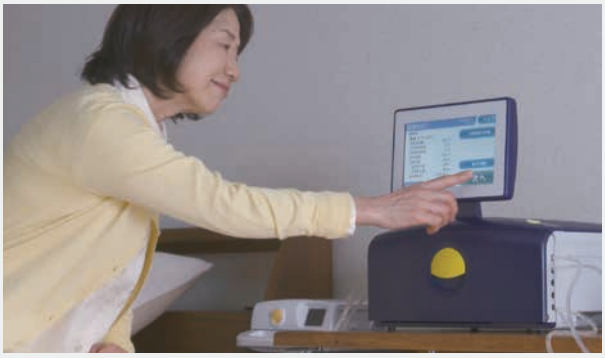
The principle of dialysis is to place a semipermeable membrane between the blood and a dialysate to remove toxins in the blood by diffusing them into the dialysate. In doing so, water and other substances are moved to adjust the amount of water and replenish deficiencies in the blood. A medical device equipped with this dialysis membrane is called a dialyzer. It substitutes the kidney's filtration function, and acts as a substitute kidney for patients with decreased kidney function. Dialysis that used this mechanism is called hemodialysis, and it is performed at medical institutions including clinics.

Peritoneal dialysis and remote monitoring

Another renal replacement therapy is peritoneal dialysis that uses the peritoneum lining of the organs in the abdomen as a dialysis membrane. In this procedure, the abdomen is filled with dialysate via catheter and the blood is purified in the body. As this can be performed at home, patients have to visit hospitals only about once a month. As such, patients can undergo dialysis treatment while continuing working without major lifestyle changes.

There are two different types of peritoneal dialysis. The first is continuous ambulatory peritoneal dialysis (CAPD), in which the bag containing dialysate is manually changed 3-5 times a day. The other is automatic peritoneal dialysis (APD) which mechanically changes dialysate at night. APD can reduce the burden of replacing dialysate during the day and allow patients more freedom of action.

The most recent technological innovations in APD allow medical staff to remotely monitor a patient's status at their home using mobile communications functions, and allow doctors to change prescriptions from hospitals.



Automatic peritoneal dialysis (APD) at home enables remote monitoring by medical staff

Paradigm shift in therapy selection

The number of dialysis patients in Japan is said to be about 330,000, and continues to increase, largely due to an aging population and increasing incidence of diabetes, which is one of the main causes for dialysis. Technological progress has improved prognosis and reduced complications such as infections. Moreover, increased treatment options such as CAPD and APD, in addition to hemodialysis, have allowed patients to choose treatments that best fit their lifestyles.

And, in Japan, the ratio of patients receiving hemodialysis to peritoneal dialysis is 97:3, which is showing the significant imbalance. This is attributed to the fact that peritoneal dialysis was not fully explained to patients because medical staff were uneasy about the procedure due to a lack of experience, and patients were concerned about self-management at home.

In recent years, there has been a call for "shared decision making" in which patients and their families fully participate in therapy selection, and we are shifting into an era where we select treatments that suit our lives and values.*

* Japan Society for Peritoneal Dialysis: Symposium in October 2017

Technological innovation that applies digital technology is set to continue in the dialysis field, such as APD remote monitoring. It is expected that medical fees and devices that offer innovative treatment will be evaluated in light of the values they offer.

Ophthalmology

The joy of seeing

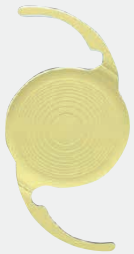
Visual disturbances significantly reduces a person's quality of life. These conditions include cataracts that affect many as they age; glaucoma, which develops in about one in 20 Japanese aged over 40; and ametropia, including myopia which has been increasingly noticed in younger aged individuals. The evolution of medical devices has given many patients the joy of seeing again with their own eyes. Here we introduce medical devices, which continue to innovate and advance the field of Japanese ophthalmology.

Cataracts: Evolving multifocal intraocular lenses

Cataracts are a condition in which the lens becomes turbid, largely due to aging. Even with modern medicine, cloudy lens cannot be restored to their original condition. Now the common method is to surgically remove lens and insert an intraocular lens. Cataracts, which were once the number one cause of blindness, are now more or less a disease which can be avoided through surgery owing to the emergence and subsequent improvements of intraocular lenses, and the development of lens reconstruction techniques for lens insertion.

The intraocular lens was introduced in 1949 by British ophthalmologist Harold Ridley. The idea of creating an intraocular lens with polymethyl methacrylate (PMMA) was inspired from pilots who sustained eye injuries from fighter jet PMMA windshield fragments, and did not show signs of foreign body reaction. It was 1985, some 36 years later, when Japan approved intraocular lenses.

The evolution of intraocular lenses over the past decade, especially multifocal intraocular lenses, have allowed not only lenses that offer far and near focus, but also diversified selection of lenses according to individual lifestyles. It is possible to select the lenses that best suit our needs after consultation with our optician; such as reading, crafting, using a computer, and improving astigmatism.



Multifocal intraocular lenses

Cataract surgery is no longer just the replacement of a cloudy lens with a clear lens. It would be no exaggeration to say that the surgery is now an opportunity to think about how to improve one's quality of life. The multifocal intraocular lens will continue to evolve as a device with the potential to expand the joy of living and seeing.

Glaucoma: Implants that expand surgical treatment options

Glaucoma may develop due to increased intraocular pressure, or in normal intraocular pressure. But in both cases, the visual field narrows due to damage to the optic disk where the optic nerve gathers. If it progresses, vision may eventually be lost. As the optic nerve is not restored to its original condition, the most important thing is to delay progression of the condition through early detection and early treatment. Recent advances in diagnosis and treatment have made it possible to reduce the risk of blindness.

Guidelines for diagnosis and treatment have been published by the Japan Glaucoma Society. The basis of treatment is continuous pharmacotherapy with eye drops. However, should the condition continue to worsen, then various surgical operations are approved as indications. In 2011, a device called a tube shunt (implant) for draining aqueous humor from the eye and prevent an increase in intraocular pressure was introduced from overseas and approved. The tube shunt is a gift for patients with problematic conditions that cannot be treated with conventional glaucoma surgery.

Silicone plate (left) and tube (right) used for tube shunt surgery.
The area of the oval plate is 350 mm², and the tube is an extremely small device with an outer diameter of 0.38 mm and an inner diameter of 0.05 mm.

The evolution of contact lenses

Contact lenses (CL) are designated as highly controlled medical devices. They are defined as "medical devices that require proper management as they may materially affect health and life in the event of adverse reactions or malfunction of devices."

The market for silicone hydrogel CL has been growing in recent years. Silicone is a material with a very high oxygen permeability, but essentially hydrophobic. For CL, in which high hydrophilicity is essential for comfort, developing products using silicone was deemed problematic. However, progress in surface treatment technology at CL manufacturers allowed the launch of products that combine high oxygen permeability and hydrophilicity on the lens surface, and they are now the mainstream. Over the past decade, an array of products that leverage these new materials and better manufacturing technologies have been developed in those technologically high-value-added products including CL for astigmatism and CL for presbyopia. Particularly in Japan, the world's most aged society, the importance of CL for presbyopia is expected to increase in the future.

Meanwhile, colored CL, which make the pupils look larger, are popular among women. In this field, products made of materials in the former generation using older coloring technology are still available on the market. The challenge now is to raise awareness, encourage correct usage, promote the use of highly safe products, and ensure eye safety among colored CL users.

Reference

The Japan Glaucoma Society Guidelines for Glaucoma (3rd Edition) addendum: Guidelines for Glaucoma Tube Shunt Surgery
http://www.nichigan.or.jp/member/guideline/glaucoma3_1.pdf

Chapter
5

The Road Ahead

Prologue

In 203X, in a village in Akita Prefecture, lives alone an 87-year-old widow, Ms. Yoshino. Her husband passed away 10 years earlier. The number of private farmers is decreasing, and agricultural corporations are becoming larger and franchised. Mechanized farming and user interfaces continue to evolve, and elderly people who are not good at picking up new things are working as long as they have physical strength and can ride on the waves of mechanization. Ms. Yoshino also intends to work until she can't anymore.

In recent days, her chest pain and shortness of breath have grown worse. She has not quite fainted, but she sometimes feels like she's descending in an elevator. A general health check that she took several years ago showed mild calcification and regurgitation in her heart valve, and she was told to see a doctor immediately if such symptoms arose. Ms. Yoshino, who had never been ill until the age of 80, had an artificial joint replacement about 5 years ago because her hip joint was degenerating and she found walking difficult. She found the artificial joint convenient. Ms. Yoshino did not hesitate in booking a medical examination because she knew from past experience that preventative treatment led to a better quality of life.

She is off to the Akita Medical Center in an autonomously driven pod. The center is 30 km, around 40 minutes away. She safely arrives soon. Autonomous driving is not fully approved, but its use is allowed in areas where there is little public transportation. Multifaceted benefits of the pod are being acknowledged; addressing the driver shortage, the withdrawal of the aged into their homes, and a lack of infrastructure, as well as improved convenience. The area has been designated as a "Special zone for social infrastructure safeguard". The pod is a means of transport for local residents, and a pod-type unmanned convenience store circulates so that the aged are not locked out from their necessary daily shopping.

Ms. Yoshino saw her doctor yesterday afternoon. Thanks to the 5G communication network, she sees her doctor from her home. For an hour and a half, including a break, nurses (coordinators), and AI Doctor Holmes asked her questions, followed by a physician's confirmation inquiry. Ms. Yoshino is asked about her daily routine and diet in detail, and her eldest daughter time to time intercepts via the Internet. Ms. Yoshino is grateful that Holmes' questions were in audio and on a screen.

Immediately after reception at the medical center, her examination begins. She takes a blood test and diagnostic imaging tests with the help of a coordinator. Ms. Yoshino's second daughter, who lives in Morioka, also arrives. Meanwhile, her eldest son living in Tokyo also participates online. The results of each test and Holmes' findings are handed in to the attending physician. The 80-year-old doctor looks over them carefully and shows Ms. Yoshino her treatment options. Unlike the past, now the doctor looks at her in the eyes when speaking to her. Her eldest son comments that he's happy to see the AI recognizes the contents of the conversation and display them with pictures on the screen. Seeing is believing, especially for Ms. Yoshino, who has become hard of hearing.

After a brief explanation, data and treatment courses of past patients with similar heart lesions are presented to Ms. Yoshino for each treatment option. They are data accumulated from the past three years up to the previous month in Japan. Laymen can't understand it. But Ms. Yoshino feels relieved to hear that the probability of complications is just as low as when she underwent the artificial joint replacement. No matter which treatment Ms. Yoshino chooses, the co-payment will be about the same (Note: the amount of co-payment in the national health insurance system. The total expense of follow-up medical treatment and hospital admission expenses are shown to the patient). Upon that advice, Ms. Yoshino decides to have a smart implant (self-diagnosing artificial organ with a sensor connected to the hospital) embedded in the heart through a minimally invasive procedure, which allows for early discharge. Although a patient can go home on the following day, preparation is required. Ms. Yoshino reserves her operation three days later when an experienced doctor in his fifties is available for the operation. After her reservation is complete, Ms. Yoshino is finished with her pre-operative examination.

1. AMDD's path

The innovation in medical technology is amazing. Thus far, it has already contributed so much toward many aspects, such as patient outcomes and reduced workload of doctors. The AMDD has worked hard under a mission to deliver world-class medical technology to Japanese patients.

AMDD's mission is "Enabling a Healthier Japan". This needs some explanation. AMDD comprises of Japanese companies affiliated with large multinational players.

In most cases, the scope of business operations of those companies is limited to Japan. Therefore, our mission is to stably supply medical devices and technology to Japanese patients, and to deliver our member's superior product technology to Japanese patients ahead of other countries. Our important role in pursuing these missions is to propose to parent companies what is necessary to meet Japanese healthcare needs and to get investments. And for sound corporate activities, we cast a keen eye on Japan's healthcare system, the soundness of social security finances, and the sustainability of financial resources.

AMDD activities are concentrated on three axes. The first is to make recommendations for the accelerated and appropriate introduction of medical devices and IVD into Japan. Second is our role as a window to the government. And third is to convey the value of advanced medical technologies.

Our major achievements over the last decade are wide-ranged, including eliminating device lag and device gap, contributing towards the formulation of the Pharmaceutical and Medical Device Act (Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices), and raising awareness of medical devices. Achievements of our member companies are also diversified, including safe and stable supply of medical devices, detailed information provision, enhancements, refinement and improvements for more effective and safe products, introduction of innovative medical devices and IVD, domestic research and clinical development, production, and procurement.

Over the last decade, awareness of medical devices has been raised, yet it is far from sufficient. Differences between medical devices and pharmaceuticals have been disseminated among relevant parties, especially in terms of the background of development (development in which feedback based on the opinions of the doctors and the results of patients' treatments are reflected in new versions of products, refinement, improvement, and the learning curve necessary for physicians). Additionally information about how they contribute to medical care (minimally invasive early hospital discharge, early recovery, improvement of QOL), and their characteristics (few in quantity but an array of types, size, combined use, and fast innovation cycle) has also been disseminated. In that respect, there are more active and fruitful discussions about the future direction of the medical device field among stakeholders such as the MHLW, the PMDA, the Japan Medical Association (JMA), insurer organizations, and clinical academic societies.

The near-future depicted in this chapter's prologue factors in the aging society and regional responses to it, progress of AI/ICT/IoT, development of autonomous driving and communication infrastructure, and innovation in medical technology itself. The intention was to depict the onset of the disease to its treatment for the patient while considering the shared decision making between the patient and the doctor. (Please read the epilogue for the path to recovery.)

Although the technology is not omnipotent, we described what the technology may bring: correction of the working environment of physicians, addressing the shortage of physicians, and task-shifting to AI. The evidence accumulated in the clinical setting and from epidemiological surveys is enormous. As we move forward, such clinical information, papers and big data will be increasingly enriched. The vastness of the latest knowledge is beyond what a single physician can handle in his/her daily interaction with patients. Thus, collaboration between doctors and AI will be a major subject.

2. What can the AMDD contribute to the future?

Do you know how big innovators in the world now capture opportunities for their innovation? Let us look at one example.

The world's population is approximately 7.5 billion, increasing by about 70 million every year. For the sake of clarity, let's assume the population will be 7.7 billion in the near future, of which about 700 million people will enjoy advanced living standards. To deliver advanced living standards to the remaining 7 billion people, goods and services must be offered at lower cost and scaled up 10 times. Yet, on the other hand, CO_2 emissions need to be reduced from the viewpoint of sustainability and energy consumption. To put it another way, big innovation must provide more than 10 times its current efficiency and added value. The existing technology and industry paradigms will be replaced with new ones. Although it is a painful process, declining industry and the disappearance of certain industrial segments will result. That's why it is called "disruptive innovation." A frequently cited example is when in 2010, the US government reported the number of electric vehicles that were estimated to be produced in 2035, which was achieved by Tesla in 2015, 20 years ahead of the estimate. For taxi drivers and the existing automotive industry, coupled with Uber, this trend is leading to disruptive innovation. Big innovation targets communication, transportation, energy, food, education, and of course, healthcare. How can the healthcare system that is currently enjoyed by 700 million people worldwide and the state-of-the-art medical technology enjoyed by an even smaller number of people be delivered to the remaining 7 billion people on the planet? (and how can any solution to this question generate further innovation and added value to build a competitive edge in the markets of the 700 million?) This is where big business opportunities lie and innovation competition is ongoing.

Column 1 Aging population

People aged 65 or older are expected to be on the rise until 2045 [1]. From 2005, we entered a phase of population decrease in which the number of deaths surpassed the number of births. In 2016, the number of newborns was below 1 million [2] (**Figure 1**).

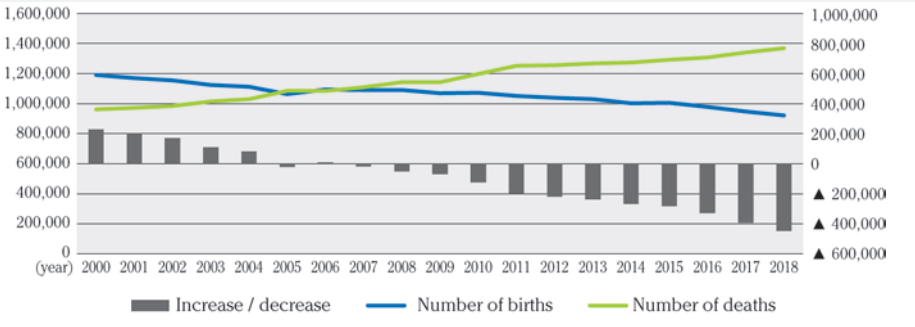


Figure 1.
Number of births and deaths (persons: left axis) and changes in increase / decrease (persons: right axis) [2]

Additionally, the number of elderly living alone has increased, and 40% of elderly people are estimated to be living alone in 2035 (**Figure 2**).

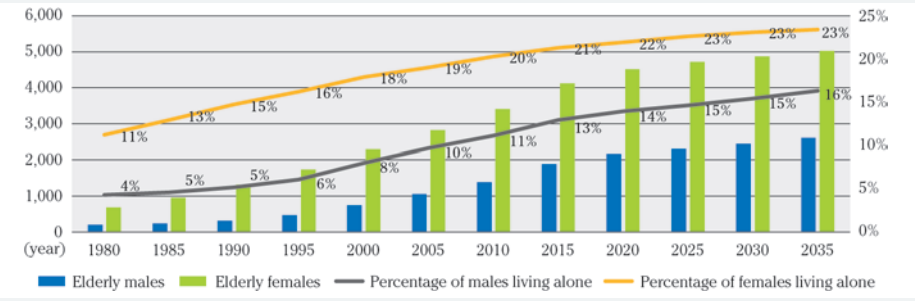


Figure 2.
Changes in the number of elderly people living alone (thousands: left axis) and percentage of all elderly people (right axis) [3]

Aging of healthcare providers

The decrease of the working generation due to aging will also affect medical professionals. Some suggest the era of elderly patients being treated by elderly medical professionals (physicians, nurses, and paramedics) could be on its way out.

The age-based structure of hospital doctors in 2006 showed that a majority of physicians were over 40 years old and the average age in 2016 was 44.5 years old, revealing an aging trend among physicians (**Figure 3**).

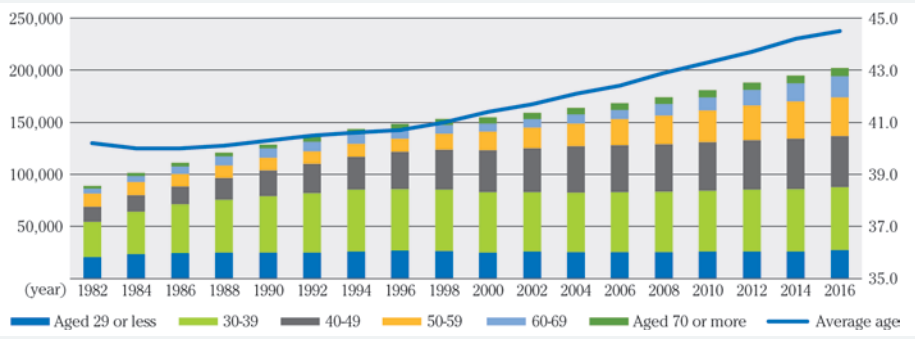


Figure 3.
Age structure of hospital doctors (persons: left axis) and average age (years: right axis) [4]

This trend is significant for those in clinics, where although the average age is 59.6 years, the number of those over 70 years accounts for 22.8% [4].

Moreover, the number of young physicians (aged 39 or less) who take over the skills of experienced physicians has leveled off. A lack of succeeding physicians has put the handing down of skills and technical know-how at risk. Amid such challenges, medical devices are expected to play a significant role in maintaining and improving clinical outcomes.

Elderly people's assets and reduced liquidity

The number of patients with cognitive decline due to aging is expected to increase. When a patient shows cognitive decline, their assets are managed by a Guardian as per the adult guardian system. In most cases, such assets are managed as deposits not to be damaged and this means they could not be invested in the market as there is risk (hence these assets become dead assets).

The total financial assets of elderly people with cognitive decline was estimated to be 127 trillion JPY in 2015 (**Figure 4**), and will exceed 200 trillion JPY by 2030.

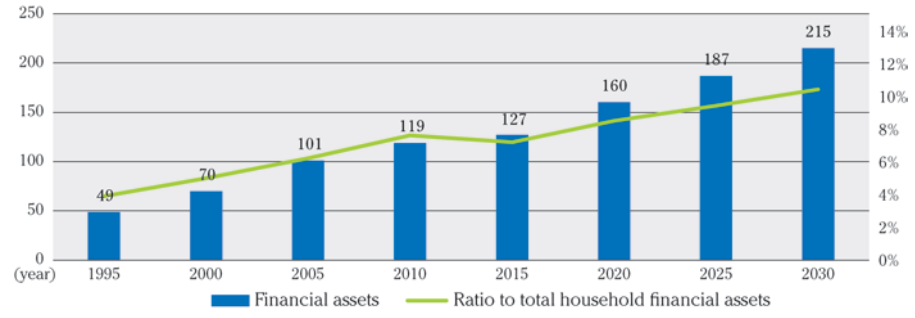


Figure 4.
Financial assets held by patients with cognitive decline (estimate and future pro forma figure: trillion yen)[5]

When compared with Japan's National Budget in FY 2019 (approx. 101 trillion) and the outstanding currency issued at the end of FY 2018 (110.4 trillion[6]), a considerable amount of money is lying dormant without underpinning the economic activity in Japan. Because of concerns over healthy life spans, those assets are hardly spent, thereby affecting the national economy.

What about the healthcare challenges in Japan? This is discussed in three key words; aging population, sustainability of financial resources, and extension of healthy life span. (See the columns for more details.) In other words, how to provide prevention, diagnosis, and treatment of diseases for healthy living at minimum additional cost to those living in various parts of Japan with limited economic power and declining mobility. An aging population results in decreased medical literacy. The number of elderly people living alone like Ms. Yoshino is increasing. The rapid development of technology and the onset and progression of dementia are testimonies to the fact that medical literacy among the aged cannot keep up.

It is extremely difficult to find solutions for the three key concepts in the current paradigm because they contradict one another. Cash hidden away by the elderly lies outside the economic cycle. An important question is how to bring that money back into the economy. Another pressing issue is whether a mechanism to channel money into healthcare can be built.

Japanese healthcare issues and the direction of big innovation are very similar. Providing the healthcare system, that Japan takes pride in, to the elderly population, which is aging and thus is becoming relatively less medically literate, is equivalent to delivering healthcare enjoyed by 700 million people to 7 billion people. There are different challenges, but answers which are applicable to both issues may emerge. Such challenges include the following cases: medical care in developing regions with poor social infrastructure; medical care for Japanese rural residents whose social infrastructure is dwindling; support for areas in which there is no room for capital investment; and support for areas where capital investment is made but nobody is using it.

These aspects elucidate the important role of the AMDD. How can we use big innovation that can solve global challenges to improve Japanese healthcare? AMDD members must be keenly aware of such question and be a good judge to carry out our mission to "Enabling a Healthier Japan".

Individual member companies will undoubtedly obtain such innovation. The role of the AMDD is to make recommendations for the accelerated and appropriate introduction of such innovation in Japan and to disseminate the value of innovation. This has been our role to date. Another important role for us going forward is to keep the global innovation community posted on Japanese business opportunities in an easy-to-understand manner, together with the government and academia.

Of course, it is important to commercialize and disseminate Japanese know-how and innovation as Japan's population becomes super-aged. An important point in finding a solution to the problem of Japanese healthcare provision must be to have innovation funded by mega-VC firms targeting 7 billion people, and to raise Japan-specific innovation as a solution for a global problem.

3. All stakeholders united

The AMDD is proud of its success in improving medical technology and contributing to patient care in Japan. This success is the result of the efforts of our member companies and their introductions of innovative technologies, and the understanding and cooperation of the MHLW, PMDA, JMA, insurers, and clinical societies.

As we head towards a society in which population growth has peaked and medical health care can no longer be provided at prices offered to date, we face a question of how to proceed. As in the development of medical devices, policy will depend on revisions and improvements brought about by drastic and disruptive innovation for all concerned.

Our aim is brighten our future through the continued development of cooperative relationships that enable patient-centered sincere discussions in these areas so that Japan's social security system can be improved.

The world depicted in the prologue and epilogue is drawn on the basis of a mechanism that is already feasible. With one eye on our changing world, I hope we can keep working hard so that a more advanced future will arrive soon.

Epilogue

While being drowsy from local anesthesia and sedatives, the surgery was over in no time. After being examined in the recovery room, Ms. Yoshino practices walking in the evening

Column 2 Sustainability of financial resources

Financial outlook in Japan

General accounts for FY 2019 exceeded the 100 trillion yen for the first time. Social security expenses including medical expenditure, ran to approximately 34 trillion yen, due to the aging population, accounting for the largest government expenditure (**Figure 5**).

The total new government bonds issued (approx. 32.7 trillion yen) exceeds the redemption amount (23.5 trillion yen), and approximately 9.2 trillion yen outstanding bonds are expected. The debt at the end of FY2019 would be 896.7 trillion yen, which is 158.4% of GDP [7]. Difficult financial circumstances are expected to continue (**Figure 6**).

Efforts toward optimized social security costs

Social security costs, especially optimized and sustainable medical costs, remain a major discussion point in Japan. Further discussions on our aging society is needed to secure medical access while looking for ways to contain the natural increase of costs.

There is room to look for more efficiency in fields such as surgery, which consumes a lot of medical resources. According to Berwick et al. [8], of the medical resources consumed in 2011, approximately 34% (US $910 billion) was inefficiently consumed. Although advanced functions across hospitals and clinics are available, medical resources are inefficiently consumed. In Japan, further consideration for efficient medical operations (lean operations) should be considered.

More than 100 billion JPY in costs, combining medical devices and pharmaceuticals, have been cut at every revision. However, we have come to a point where it is no longer possible to look for further reductions in the cost of medical devices / pharmaceuticals. Guidelines on cost-effectiveness have already been issued, but there is a need for further discussion, not only on the incremental cost-effectiveness ratio (ICER), but also on avoiding risks in nursing care, for which medical devices are useful, and avoiding the risk of productivity loss in the future.

In the 2018 medical fees revision, a stepped reimbursement scheme was introduced for basic inpatient fees by the beds' functional category depending upon actual accepted number of acute phase patients. However, in Japan, still the number of beds for acute phase patients is significantly high and this does not well reflect for the future demand of distribution for nursing or chronic phase beds due to the aging society (**Figure 7**).

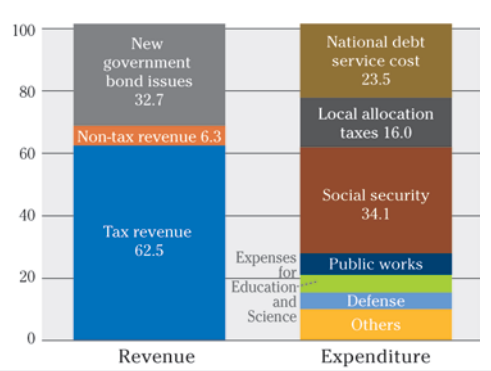


Figure 5. General account for FY 2019 (trillion yen)
101 trillion 456.4 billion yen

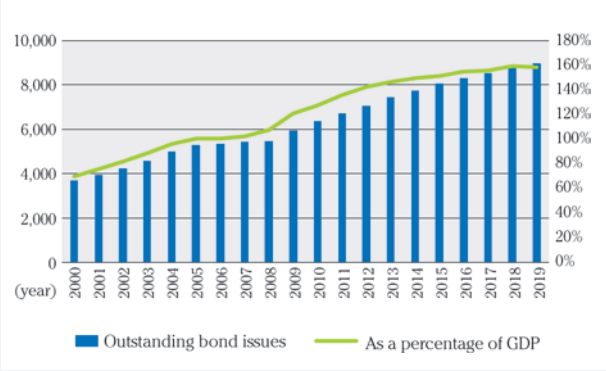


Figure 6. Outstanding bond issues (trillion yen) after 2000 and as a percentage of GDP [7]

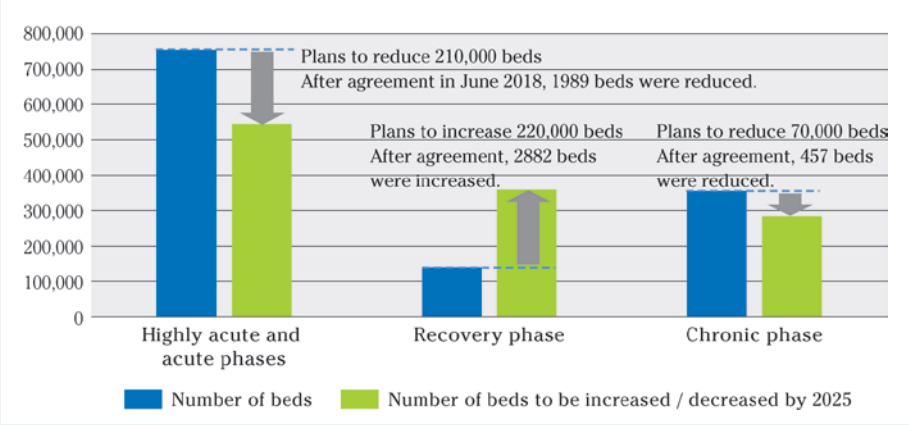


Figure 7. Number of hospital beds by function (2016) [9), 10)]

without a problem. She is informed that the operation was a success, and she is to be discharged. Her second daughter, who accompanied her, also feels relieved. As planned, Ms. Yoshino stays overnight at a hotel she reserved with postoperative support service near the hospital because she is a little worried. If something happens, there is a nurse on call so she can feel safe and secure. The smartphone in the room has a monitoring app and an AI doctor, which addresses voice inquiries other than stressed or panic-stricken voices. The state of the implant and the patient's body are also monitored.

Ms. Yoshino stayed overnight without incident, and went to the hospital the next morning. She received a final confirmatory interview with the nurse, paid electronically, and returned home. The itemized expenses received by e-mail detail the total amount in yen along with the amount she had to pay. This is part of the recent efforts to raise awareness of medical expenses. Ms. Yoshino was surprised to see the total amount, but remembers her eldest son telling her about the High-Cost Medical Expense Benefit. She is indeed grateful to the national health insurance system. Ms. Yoshino is given a watch-like monitor from the hospital for postoperative management.

The monitor, which is connected to the medical center's monitoring room via a smartphone app, is provided in case of the need for intervention. The monitor will be removed in a month, but Ms. Yoshino wants to buy a similar monitor and continue to focus on her farming work while self-managing her health.

Column 3 Extension of healthy life span

Changes in healthy life span and average life expectancy

The length of unrestricted daily life (healthy life span) and average life expectancy are extending. Since a 2001 survey, healthy life span has extended by 2.74 years for men and 2.14 years for women [11].

In the 2011 survey by the OECD, numerical thinking and reading comprehension skills of Japanese were above the international averages. There is growing expectation for senior citizens to continue their active participation in society (**Figure 8**).

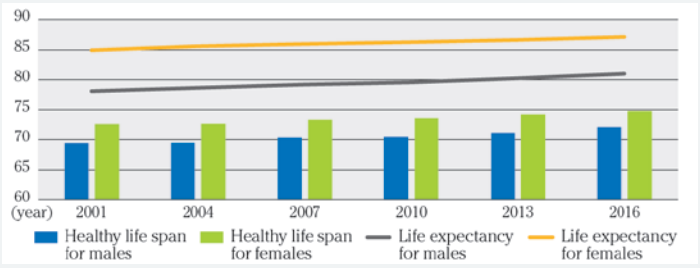


Figure 8. Changes in healthy life span and average life expectancy [11]

Older retirement ages

The regular retirement age is significantly shifting to a higher age. In 1986, efforts were made to introduce a retirement age of 60, and this became legally enacted in 1998. Simultaneously, efforts to change the retirement age to 65 began. In 2012, the Japanese government enacted a retirement age of 65 for workers to be entitled to benefits; but workers are permitted to work beyond the retirement age (**Figure 9**).

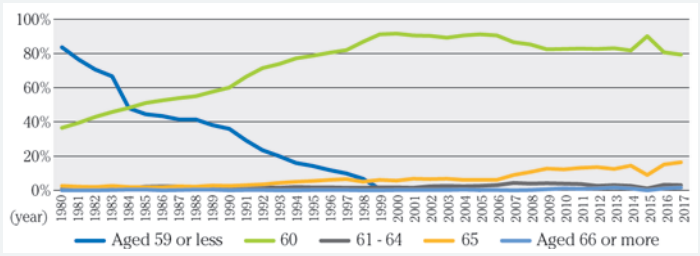


Figure 9. Changes in the corporate retirement age [12]

Raising the elderly employment rate

The elderly employment rate has increased by about 5 points from 2008 (male: 19.7%, female: 12.8%) to 2018 (male: 24.3%, female: 17.4%) (**Figure 10**).

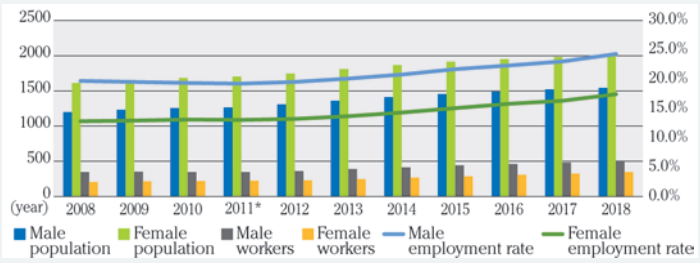


Figure 10. Changes in the total working population over the age of 65 (10,000 persons: left axis) and employment rate (right axis) [13] *: Estimated value

Reference

1) 2017 White Paper on Aging Society (Cabinet Office: Https://www8.cao.go.jp/kourei/whitepaper/w-2017/html/zenbun/s1_1_1.html)
2) 2018 Annual estimates of demographic statistics (MHLW: Https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/suikei18/index.html)
3) 2016 White Paper on Aging Society (Cabinet Office: Https://www8.cao.go.jp/kourei/whitepaper/w-2016/html/zenbun/s1_2_1.html)
4) 2016 Doctor, dentist, pharmacist survey overview (MHLW: Https://www.mhlw.go.jp/toukei/saikin/hw/ishi/16/index.html)
5) The future of dementia patient with financial assets worth 200 trillion yen (Dai-Ichi Life Research Institute Inc.: Http://group.dai-ichi-life.co.jp/dlri/pdf/macro/2018/hoshi180828.pdf)
6) Tell me! BOJ (Bank of Japan: Https://www.boj.or.jp/announcements/education/oshiete/money/c06.htm/)
7) Changes of post war government bond management policy (Ministry of Finance: Https://www.mof.go.jp/jgbs/reference/appendix/hakkou01.pdf)
8) Berwick D.M., Hackbarth A.D., Eliminating Waste in US Health Care, JAMA. 2012;307(14): doi: 10.1001/jama.2012.362
9) Results of 2016 report on the function of hospital beds (MHLW: https://www.mhlw.go.jp/file/05-Shingikai-10801000-Iseikyoku-Soumuka/0000164336.pdf),
10) Council on Economic and Fiscal Policy:Toward Steady Promotion of a New Economic and Fiscal Regeneration Plan - Social Security System Reform - (reference material): (https://www5.cao.go.jp/keizai-shimon/kaigi/minutes/2019/0410/shiryo_01-2.pdf)
11) 2018 White Paper on Aging Society (Cabinet Office: Https://www8.cao.go.jp/kourei/whitepaper/w-2018/zenbun/pdf/1s2s_02_01.pdf)
12) Employment management survey (MHLW: Http://www.mhlw.go.jp/toukei/list/39-16.html) and comprehensive survey of working conditions (MHLW)
13) Labor force survey (basic tabulation) (Statistic Bureau of Japan: Https://www.stat.go.jp/data/roudou/sokuhou/tsuki/index.html)

The History of the AMDD

2010

- April 1, Mr. David Powell (President of Johnson & Johnson K. K.) is appointed as the second Chairman
- April, "A Proposal from the Medical Device Industry with regard to the New Growth Strategy 'A Healthy Country through Life Innovation'" was released
- August, Position paper "Thoughts on the Handling of Invitro diagnostics" was released
- November, Proposal "Medical Device Maintenance Compliance as an Issue of Medical Safety" was released

2009

- April 1, The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) spins off from ACCJ; Dr. Huimin Wang was appointed as first Chairman (President of Edwards Lifesciences Ltd.) (Masataka Toyota, the first Staff Director), and a press conference was held
- May, Book titled "I'm glad I chose this treatment," a compilation of essays by patients who selected the latest medical technology, was published
- July, Research paper "Comparison of Medical Device Supply Costs in Japan and Europe" was released

April 2009, press release on the inception of the AMDD

May 2009, Essay Collection

July 2009, Comparison of Medical Device Supply Costs in Japan and Europe

2008

- October, "Device Lag Report" was released
- December, Press conference for "Device Lag Report"

December 2008, press conference for "Device Lag Report"

2007

- November, Media Forum titled, "Thinking about the Future of Japanese Healthcare" was held

2007 November, Media Forum titled "Thinking about the Future of Japanese Healthcare"

December 2006, press conference for the viewpoint paper on patient access

2009

2008

December 2008, MHLW launched "Medical Device Review Acceleration Action Program"

2007

2006

2006

- December, Viewpoint paper titled, "Improve Patient Access to Advanced Medical Technology" was released and press conference was held

2005

The term "device lag" comes into use.

2004

2004

- Symposium titled "Patient-Centered Medical Care" was held

2003

2003

- February, The first Media Lecture was held (subsequently held every other month)
- July, Exhibition, titled "International Modern Hospital Show 2003" was held

Media lectures commenced in 2003

International Modern Hospital Show exhibition in July 2003

2002

2002

- In October, the ACCJ Medical Device and Diagnostics Subcommittee began a public awareness campaign titled "Value of Medical Technology"

Revised Pharmaceutical Affairs Law (effective April 2005) enacted.

1999

1999

- Proposal titled "A Turning Point of the Japanese Healthcare System" was released

1997

1997

- Proposal titled "The Role of Medical Equipment and Supplies in Improving the Efficiency and Quality of the Japanese Healthcare System" was released

The 1990s

- Medical Devices and Diagnostics Subcommittee was established within the ACCJ Healthcare Committee (later renamed the Medical Device / IVD Subcommittee)

2019

- April 1, 10th anniversary of the AMDD

2018

- April, “Proposals from the Medical Device Industry for the 5th Year Revision of the Pharmaceuticals and Medical Device Act” was released.

January 2018, Press conference by Chairman to announce the establishment of the MTPI

2017

- February, Proposed “Value-Based Reimbursement System” that reflects the innovation value of medical devices and held press conference
- April, Symposium in collaboration with the Japan Medical Association (JMA), National Federation of Health Insurance Societies (KENPOREN), and the AdvaMed, “Creating a Vibrant Nation and Life Purpose” (annually held hereafter)
- October 1, Established the Medical Technology Policy Institute (MTPI), (Mr. Makoto Tamura, Director)

October 2017, Public-private discussion

February 2017, Press conference for a value-based reimbursement system

2016

- January, Change of organization status to a general incorporated association

2015

- August 1, Mr. Kosuke Kato (Managing director of Edwards Lifesciences Ltd.) is appointed as the fourth Chairman of the AMDD

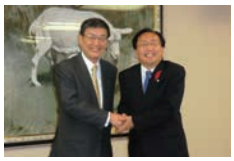
2014

- April, Book titled “I’m glad I chose this treatment II,” the second compilation of patients’ essays was published
- June, “Proposals on the Appropriate Provision of In-vitro Diagnostics” was released

April 2014, second collection of essays

2013

- June, “Proposal on Healthcare Associated Infections (HAIs) and Healthcare Worker Safety” was released
- October, Participation and exhibition at Aomori Prefecture and AMDD Collaboration forum, “Collaboration of Medicine and Engineering to Open up a New Future”



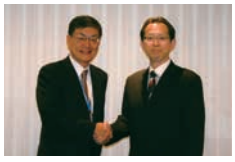
October 2013, Courtesy Visit from the Aomori Prefectural Governor at the AMDD Collaboration Forum

November 2013, “Pharmaceutical and Medical Device Act” (PMD Act) enacted (Executed in October 2014)

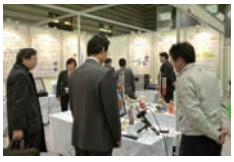
2012

- April 1, Mr. Takashi Shimada (President of Medtronic Japan Co., Ltd.) is appointed as the third Chairman (Hiroshi Ikeda, the second Staff Director)
- June, “Proposal on Healthcare Associated Infections (HAIs) and Healthcare Worker Safety” was released
- August, Participation in Children’s Government Offices Field Trip Day (annual participation hereafter)
- November, “Medical Creation Fukushima 2012” exhibition
- December, “Research on the Economic Evaluation of Large Medical Devices” report was released

August 2012, booths at Children’s Government Offices Field Trip Day



October 2012, Courtesy visit to the Fukushima Prefectural Deputy Governor



November 2012, Medical Creation Fukushima 2012

March 11, 2011, Great East Japan Earthquake

2011

- July, “Proposal for Revisions to the Pharmaceutical Affairs Law for Medical Devices” and “Proposal for Revision to the Pharmaceutical Affairs Law for IVDs” were released
- August, “Opinion Survey of Japanese Healthcare and Advanced Medical Technology” report was released and press conference was held
- September, “Comparison Survey of Market Environment for Medical Devices in Japan, China, and Korea” was released and press conference was held
- November, “Proposal on Infrastructure Building for Companion Diagnostics for the Promotion of Personalized Medicine” was released

August 2011, “Opinion Survey of Japanese Healthcare and Advanced Medical Technology”

September 2011, “Comparison Survey of Market Environment for Medical Devices in Japan, China, and Korea”

Profile of the AMDD

The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) is an industry group founded in 2009 consisting of approximately 70 Japanese corporations that handle medical devices and in-vitro diagnostics (IVD), with headquarters located mainly in the United States. At the AMDD we aim to deliver the latest medical technology (treatment and diagnostic technology) and information to meet the needs of medical setting and patients in Japan. Our member companies not only import and sell products, but also work closely with the Japanese medical device industry in research and development and manufacturing, and actively use components developed and manufactured in Japan in their products. Furthermore, our member companies account for about 70% (about 1.8 trillion yen) of domestic sales of medical devices, and have created approximately 27,000 jobs (as of 2019) as direct employment in Japan. Their domestic bases, including repair and maintenance facilities, spread to almost all prefectures and contribute to the development of the Japanese medical device industry.

AMDD's Mission

To provide valuable medical technology and information for the healthy everyday lives of people.

Activities of the AMDD

1 Providing recommendations to facilitate fast and appropriate introduction of medical devices

AMDD offers recommendations to the Japanese government regarding regulatory systems for the fast and safe introduction of the world's advanced medical technologies to Japan. Such recommendations are provided in cooperation with the US government and the US-based Advanced Medical Technology Association (AdvaMed).

2 Serving as a contact to the government

In order to realize overall cut backs on medical costs and appropriate allocation of healthcare expenditures, AMDD serves as a point of contact between member companies and government offices such as the Ministry of Health, Labour and Welfare, with regard to the reimbursement system and related regulatory revisions.

3 Communicating the value of advanced medical technology

AMDD undertakes a variety of activities intended to inform a wide range of people, including the media, government officials and politicians, medical professionals, and the general public of the value and role of advanced medical technologies.

Executive Committee (as of April 1, 2019)

Chairman
Kosuke Kato (Managing Director, Edwards Lifesciences Limited)

Vice Chairman
Yusuke Naiki (Chairman, Boston Scientific Japan K.K.)
Tony Semedo (President of Medtronic Japan Co., Ltd.)

Directors
Tatsuo Achiwa (President & Representative Director, Nippon Becton Dickinson Company, Ltd.)
Sotaro Amano (Representative Director and Chairman of the Board and President, Abbott Japan Co., Ltd.)
Samih Al Mawass (President & Representative Director, Abbott Vascular Japan Co., Ltd.)
Ryo Noda (President, Asia Pacific, Cardinal Health)
Kazuya Ogawa (Chairman & President, Zimmer Biomet G.K.)
Danny Risberg (President, Representative Director, Baxter Ltd.)
Hiroyuki Saeki (Representative Director and President, Stryker Japan K.K.)
Soichiro Tada (President & CEO, GE Healthcare Japan Co.)
Takanao Tamai (President, Johnson & Johnson K.K.)
Masaaki Tsuchimoto (President, Abbott Medical Japan LLC, Head of CAHF)

Auditors
Shigeyuki Masukawa (Vice President, Boston Scientific Japan K. K.)
Koichi Higuchi (Koiichi Higuchi, CPA, Tax Counselor)

Advisors
Takashi Shimada (Former President of Medtronic Japan Co., Ltd.)
Toshifumi Hayashi (Director, Government Affairs, Edwards Lifesciences Limited)
Marie Kissell (Senior Advisor, Government Affairs, Abbott Japan Co., Ltd.)

Director, Medical Technology Policy Institute (MTPI)
Makoto Tamura (Representative Director and CEO, Healthcare System Planning)

Staff Director
Hiroshi Ikeda

Member Companies (As of December 31, 2019)

3M Japan Limited Health Care Company
Abbott Diagnostics Medical Co., Ltd.
Abbott Japan LLC
Abbott Vascular Japan Co., Ltd.
Abbott Medical Japan LLC
Abiomed Japan K.K.
Accuray Japan K.K.
Alcon Japan Ltd.
Allergan Japan KK
AMO Japan K.K.
Arthrex Japan G.K.
Asahi Kasei Zoll Medical Corp.
Avanos Medical, Inc.
Bausch & Lomb Japan Co., Ltd.
Baxter Ltd.
Bayer Yakuhin, Ltd.
Biosensors Japan Co., Ltd.
Biotronik Japan, Inc.
Boston Scientific Japan K.K.
Cardinal Health Japan G.K.
Century Medical, Inc.
Cook Japan, Inc.
Cooper Vision Japan, Inc.
Edwards Lifesciences Ltd.
Exactech K.K.
GE Healthcare Japan Co.
Haemonetics G.K.
Hollister Co., Ltd.
Hologic Japan Inc.
InSightec Japan K.K.
Intuitive Surgical G.K.
Japan Lifeline Co., Ltd.
Japan Medicalnext Co., Ltd.
Johnson & Johnson K.K.
KYOCERA Co.
LabPMM Japan G.K.
Lumenis Japan Co., Ltd.
Masimo Japan Co.
Medacta Japan Co.
Medicon Inc.
Medline Japan G.K.
Medtronic Japan Co., Ltd.
MicroPort Orthopedics Japan K.K.
Murata Manufacturing Co., Ltd.
Nova Biomedical K.K.
Nippon Becton Dickinson Company, Ltd.
Nippon Covidien Ltd.
O&M Halyard Japan G.K.
Ortho-Clinical Diagnostics K.K.
Otsuka Medical Devices Co., Ltd.
Philips Japan, Ltd.
ResMed KK
Sakura Global Holding Co., Ltd.
Smith & Nephew KK
STERIS Japan Inc.
Stryker Japan K.K.
Thermo Fisher Diagnostics K.K.
TKB Co.
Ultradent Japan K.K.
Varian Medical Systems K.K.
Vorpal Technologies K.K.
Zimmer Biomet G.K.

Associate members

Avery Dennison Japan K.K.
Mars Tohken Solution Co., Ltd.
Nippon Express Co., Ltd.
North American Science Associates Japan G.K.
NTT DATA Corporation
NTT Logisco Inc.
SATO HEALTHCARE CO., LTD.
SEAOS, Inc.
Sunmedix Co., Ltd.
Toppan Forms Co., Ltd.
Yamato Logistics Co., Ltd.

Executive Committee (April 2019)

AMDD 10th Anniversary
Memorial Book:
AMDD 10-year
History and Beyond

Publication date:
February 1, 2020

Planning and publication:
AMDD 10th Anniversary
Memorial Book Committee

Editing and production:
Cosmo Public Relations Corporation

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Among the articles in this book, the pieces on 10 Years of Innovation Saving Patients regarding each disease field, were written and contributed to by member companies that have medical technology related to the relevant field, and by committees within the AMDD. We would like to thank the authors of each chapter and the companies they represent. We would also like to express our sincere gratitude to everyone who has been supporting the AMDD since the time when it was part of the ACCJ Medical Devices and IVD Subcommittee to the present day, and all those who took part in the round-table discussion.

American Medical Devices and Diagnostics Manufacturers' Association
Nakano Central Park South 15F, 4-10-2 Nakano, Nakano-ku, Tokyo 164-0001